Initial REMS approval: 11/2014

BLA 103948 LEMTRADA™ (alemtuzumab)

CD52-directed cytolytic antibody

Genzyme Corporation

500 Kendall Street, Cambridge, MA 02142

Phone: 1-800-745-4447

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL

The goal of the LEMTRADA REMS is to mitigate the risks of autoimmune conditions, infusion reactions, and malignancies associated with LEMTRADA by:

Helping to ensure informed decisions about the safe use of LEMTRADA by:

- Informing patients about the serious risks of autoimmune conditions, infusion reactions, and malignancies with LEMTRADA and the need for baseline and periodic monitoring; and
- Informing healthcare providers about the serious risks of autoimmune conditions, infusion reactions, and malignancies with LEMTRADA, the need to counsel patients, and the need for baseline and periodic monitoring.

Helping to ensure the safe use of LEMTRADA by:

- Ensuring that only certified prescribers prescribe LEMTRADA;
- Ensuring that LEMTRADA is dispensed only in certain healthcare settings, by certified pharmacies, and certified infusion sites, which have on-site access to equipment and personnel trained to manage infusion reactions; and
- Ensuring that only enrolled and authorized patients receive LEMTRADA;
- Ensuring that certified prescribers submit documentation of periodic monitoring of patients who receive LEMTRADA to identify autoimmune conditions and malignancies

II. REMS ELEMENTS

A. Communication Plan

Genzyme will implement the following communication plan to healthcare providers likely to diagnose, treat, and manage patients with multiple sclerosis. The communication plan will include:

1. REMS Letter for Healthcare Providers

Genzyme will send a *REMS Letter for Healthcare Providers* within 60 days of approval of the LEMTRADA REMS and again at 12 months, 24 months, and 36 months from the date of the REMS approval. The REMS Letters will address the risk of autoimmune conditions, infusion reactions, and malignancies associated with LEMTRADA as well as support the implementation of the LEMTRADA REMS program. A copy of or a link to the Prescribing Information will accompany each *REMS Letter for Healthcare Providers*.

Genzyme will use email as the primary method to disseminate the REMS Letter. If an email is marked as unopened, Genzyme will send a second email within 30 calendar days. If the second email is marked as unopened, Genzyme will mail the REMS Letter within 30 calendar days. If an email address is not available or if the email is undeliverable, Genzyme will mail the REMS Letter within 30 calendar days.

Genzyme will send the *REMS Letter for Healthcare Providers* to prescribers who have written at least one prescription within the previous 2 years for a prescription drug indicated for the treatment of multiple sclerosis.

2. REMS Website

Genzyme will ensure that the website (www.LEMTRADAREMS.com) will be available for the duration of the REMS. Genzyme will ensure that the website will contain information on the LEMTRADA REMS and will provide access to downloadable versions of all approved REMS materials, and the Prescribing Information.

The following are part of the REMS and are appended:

- The *REMS Letter for Healthcare Providers* (print and email versions)
- The LEMTRADA™ REMS Website

B. Elements to Assure Safe Use

1. Healthcare providers who prescribe LEMTRADA are specially certified.

a. To become specially certified to prescribe LEMTRADA in the LEMTRADA REMS Program, healthcare providers must:

i. Review the Prescribing Information for LEMTRADA.

ii. Review the *LEMTRADA REMS Program Overview* and *LEMTRADA REMS Education Program for Prescribers* and successfully complete the *LEMTRADA REMS Knowledge Assessment*.

iii. Enroll in the LEMTRADA REMS Program by completing and signing the *LEMTRADA REMS Prescriber Enrollment Form* and submitting it to the LEMTRADA REMS Program.

b. As a condition of certification, prescribers must agree to:

i. Enroll each patient in the LEMTRADA REMS Program by:

1) Informing the patient about the risks associated with LEMTRADA, including the risks of autoimmune conditions, infusion reactions, and malignancies, and the need for baseline and periodic monitoring, by counselling on and providing each patient with *What You Need to Know About LEMTRADA Treatment: A Patient Guide* and a *LEMTRADA Patient Safety Information Card*.

2) Completing the *LEMTRADA REMS Patient Enrollment Form* for each patient and providing a completed copy to the patient. The completed form must be submitted to the LEMTRADA REMS Program and a copy should be stored in the patient's records.

ii. Submit a *LEMTRADA REMS Prescription Ordering Form* for each LEMTRADA prescription to the LEMTRADA REMS Program.

iii. Perform the baseline and periodic monitoring described in the Prescribing Information.

iv. Submit a *LEMTRADA REMS Patient Authorization and Baseline Lab Form* to the LEMTRADA REMS Program indicating completion of each patient's baseline laboratory testing within 30 days prior to the patient's infusion date.

v. Complete the *LEMTRADA REMS Patient Status Form* 6 months after the patient's first infusion with LEMTRADA, and every 6 months thereafter, until 48 months after the completion of the patient's last infusion of LEMTRADA and submit the completed form to the LEMTRADA REMS Program.

vi. Report any adverse events suggestive of autoimmune conditions, infusion reactions, and malignancies to Genzyme.

vii. Notify Genzyme if an enrolled patient who has received LEMTRADA within the last 48 months is no longer under your care.

b. Genzyme will:

i. Ensure that healthcare providers who prescribe LEMTRADA are specially certified, in accordance with the requirements described above.

ii. Ensure that prescriber enrollment and documentation of training can be submitted by fax to (1-855-557-2478) to the LEMTRADA REMS Program.

iii. Ensure that healthcare providers are notified when they have been certified by the LEMTRADA REMS Program.

iv. Maintain a validated, secure database of healthcare providers who are certified to prescribe LEMTRADA in the LEMTRADA REMS Program. Genzyme will ensure that the healthcare provider's certification requirements are met and may de-certify non-compliant healthcare providers if the requirements do not continue to be met.

v. Send a *LEMTRADA REMS Patient Status Reminder Letter* electronically or by mail 6 months after each patient's first LEMTRADA infusion, and every 6 months thereafter for 48 months, to certified prescribers enrolled in the LEMTRADA REMS Program, who must submit a completed *LEMTRADA REMS Patient Status Form* for an enrolled patient who has received LEMTRADA within the last 48 months.

vi. Provide the *LEMTRADA REMS Prescriber Enrollment Form, LEMTRADA REMS Patient Enrollment Form, LEMTRADA REMS Program Overview, LEMTRADA REMS Education Program for Prescribers, LEMTRADA REMS Patient Status Form, LEMTRADA REMS Prescription Ordering Form, LEMTRADA REMS Patient Authorization and Baseline Lab Form, What You Need to Know About LEMTRADA Treatment: A Patient Guide* and the Prescribing Information to healthcare providers who (1) attempt to prescribe LEMTRADA and are not yet certified, or (2) inquire about how to become certified.

vii. Ensure that the REMS materials listed below are available on the LEMTRADA REMS Program Website (www.LEMTRADAREMS.com) and can be accessed or by calling the REMS call center (1-855-676-6326).

The following materials are part of the REMS and are appended:

- *LEMTRADA REMS Program Overview*
- *LEMTRADA REMS Education Program for Prescribers*
- *LEMTRADA REMS Knowledge Assessment*
- *LEMTRADA REMS Prescriber Enrollment Form*
- *LEMTRADA REMS Patient Enrollment Form*
- *LEMTRADA REMS Patient Status Form*
- *What You Need to Know About LEMTRADA Treatment: A Patient Guide*
- *LEMTRADA REMS Prescription Ordering Form*
- *LEMTRADA REMS Patient Authorization and Baseline Lab Form*
- The LEMTRADA™ REMS Website
- *LEMTRADA REMS Patient Status Reminder Letter*

2. LEMTRADA is dispensed only in certain healthcare settings, by pharmacies and infusion sites that are specially certified.

a. To become specially certified to dispense LEMTRADA in the LEMTRADA REMS Program,

i. Each pharmacy must:

1) Designate an authorized representative to complete enrollment by submitting the completed *LEMTRADA REMS Pharmacy Enrollment Form* on behalf of the pharmacy.

2) Ensure the authorized representative will oversee implementation and compliance with the LEMTRADA REMS Program requirements by:

a. Reviewing the *LEMTRADA REMS Program Overview.*

b. Ensuring that all relevant staff involved in the dispensing of LEMTRADA are educated and trained using the *LEMTRADA REMS Program Overview*.

c. Putting processes and procedures in place, and following such processes and procedures, to ensure the following verifications and safe use conditions are met prior to dispensing LEMTRADA:

i. The *LEMTRADA REMS Prescription Ordering Form* is received for each prescription.

ii. LEMTRDA is dispensed to certified infusion sites only.

iii. The prescriber is certified, the infusion site is certified, and the patient is enrolled and authorized to receive LEMTRADA by calling the LEMTRADA REMS Program prior to dispensing LEMTRADA.

d. Complying with request to be audited to ensure all training, processes and procedures are in place and being followed for the LEMTRADA REMS Program and appropriate documentation is available upon request.

e. Agreeing to renew enrollment in the LEMTRADA REMS Program every 2 years from initial enrollment.

ii. Each infusion site must:

3) Designate an authorized representative to complete enrollment by submitting the completed *LEMTRADA REMS Healthcare Facility Enrollment Form* on behalf of the infusion site.

4) Ensure the authorized representative will oversee implementation and compliance with the LEMTRADA REMS Program requirements by:

a. Reviewing the *LEMTRADA REMS Program Overview* and *LEMTRADA REMS Education Program for Healthcare Facilities.*

b. Ensuring that all relevant staff involved in the dispensing and administration of LEMTRADA are educated and trained using the *LEMTRADA REMS Program Overview* and the *LEMTRADA REMS Education Program for Healthcare Facilities*.

c. Putting processes and procedures in place, and following such processes and procedures, to ensure the following verifications and safe use conditions are met prior to, during, and following dispensing LEMTRADA:

iv. The *LEMTRADA REMS Prescription Ordering Form* is received for each prescription.

v. The prescriber is certified and the patient is enrolled and authorized to receive LEMTRADA by calling the LEMTRADA REMS Program prior to dispensing LEMTRADA.

vi. Patients are counseled about the risk for infusion reactions and provided with *What You Need to Know about LEMTRADA Treatment and Infusion Reactions: A Patient Guide* prior to dispensing LEMTRADA.

vii. The infusion site is equipped with the necessary equipment and personnel to manage infusion reactions.

viii. LEMTRADA is not dispensed outside of the authorized representative's certified infusion site.

ix. Monitoring patients for infusion reactions during and for at least 2 hours after each LEMTRADA infusion.

x. Completing a *LEMTRADA REMS Infusion Checklist* for each patient at the conclusion of each treatment course and submitting by fax (1-855-557-2478) to the LEMTRADA REMS Program within 5 business days.

xi. Renewing enrollment in the LEMTRADA REMS Program every 2 years from initial enrollment.

5) Ensuring that unused vials of LEMTRADA are returned to a distributor within 50 business days from the date of submission of the *LEMTRADA Patient Authorization and Baseline Lab Form.*

6) Complying with request to be audited to ensure that all training, processes and procedures are in place and are being followed for the LEMTRADA REMS Program and appropriate documentation is available upon request.

b. Genzyme will:

i. Ensure that LEMTRADA is dispensed only by pharmacies and infusion sites that are specially certified in accordance with the requirements described above.

ii. Ensure that pharmacy and infusion site enrollment and certification can be submitted by fax (1-855-557-2478) to the LEMTRADA REMS Program.

iii. Ensure that pharmacies and infusion sites are notified when they have been certified by the LEMTRADA REMS Program.

iv. Ensure that certified pharmacies and certified infusion sites are provided access to the database of certified health care providers and enrolled patients by contacting the LEMTRADA REMS Program (1-855-676-6326).

v. Contact certified infusion sites if a completed *LEMTRADA REMS Infusion Checklist* has not been received by the LEMTRADA REMS Program within 40 days from the date of submission of the *LEMTRADA Patient Authorization and Baseline Lab Form*.

vi. Verify annually that the authorized representative is the current designated authorized representative for the certified pharmacy and certified infusion site.

The following materials are part of the REMS and are appended:

- *LEMTRADA REMS Healthcare Facility Enrollment Form*
- *LEMTRADA REMS Pharmacy Enrollment Form*
- *LEMTRADA REMS Education Program for Healthcare Facilities*
- *LEMTRADA REMS Program Overview*
- *LEMTRADA REMS Infusion Checklist*
- *What You Need to Know about LEMTRADA Treatment and Infusion Reactions: A Patient Guide*

3. LEMTRADA will be dispensed[1] to patients only in certain health care settings, specifically, certified infusion sites that have the necessary on-site equipment and personnel to manage infusion reactions.

Genzyme will ensure that LEMTRADA will only be available to be dispensed to patients in an infusion site that has the necessary on-site equipment and personnel to appropriately manage serious infusion reactions (including anaphylaxis, cardiac and respiratory emergencies) and is certified in the LEMTRADA REMS Program.

The following materials are part of the REMS and are appended:

- *LEMTRADA REMS Healthcare Facility Enrollment Form*
- *LEMTRADA REMS Infusion Checklist*
- *What You Need to Know about LEMTRADA Treatment and Infusion Reactions: A Patient Guide*
- *LEMTRADA REMS Program Overview*
- *LEMTRADA REMS Education Program for Healthcare Facilities*

[1] For the purposes of this REMS, dispensed to patients only in certain health care settings includes dispensing and administration in health care settings, specifically infusion sites.

4. LEMTRADA will be dispensed to patients with evidence or other documentation of safe-use conditions.

a. To become enrolled in the LEMTRADA REMS Program, each patient must sign a LEMTRADA REMS Patient Enrollment Form indicating that he/she has:

i. Been counselled with and provided *What You Need to Know About LEMTRADA Treatment: A Patient Guide*;

ii. Been counselled by the prescriber regarding the risks associated with LEMTRADA, including the risks of autoimmune conditions, infusion reactions and malignancies;

iii. Been counselled by the prescriber regarding the need for baseline and periodic monitoring recommendations contained in the LEMTRADA Prescribing Information;

iv. Been counselled with and provided a *LEMTRADA Patient Safety Information Card*.

b. Genzyme will:

i. Ensure that the certified prescriber is able to submit the completed *LEMTRADA REMS Patient Enrollment Form* to the LEMTRADA REMS Program by fax (1-855-557-2478).

ii. Ensure that each patient treated with LEMTRADA is enrolled in the LEMTRADA REMS Program before LEMTRADA is dispensed to the patient, by verification prior to dispensing and administration (see Section B.2.).

iii. Ensure that LEMTRADA is dispensed to patients only if there is evidence or other documentation that they have met the following safe use conditions:

1) Patients have been counselled with and provided a *LEMTRADA Patient Safety Information Card*, *What You Need to Know about LEMTRADA Treatment: A Patient Guide*, and *What You Need to Know about LEMTRADA Treatment and Infusion Reactions: A Patient Guide,* on the risks associated with LEMTRADA, including the risks of autoimmune conditions, infusion reactions, and malignancies.

2) Patients have completed the *LEMTRADA REMS Patient Enrollment Form*.

iv. Send a *LEMTRADA REMS Patient Reminder Letter* to patients enrolled in the LEMTRADA REMS Program. These monthly communications will be sent to patients who have received LEMTRADA within the last 48 months, reminding the patient to obtain the needed periodic monitoring as described in the Prescribing Information, and will include a request for the patient's preferred method of contact for receiving future monthly reminders.

The following materials are part of the REMS and are appended:

- *What You Need to Know about LEMTRADA Treatment: A Patient Guide*
- *LEMTRADA Patient Safety Information Card*
- *What You Need to Know about LEMTRADA Treatment and Infusion Reactions: A Patient Guide*

- *LEMTRADA REMS Patient Reminder Letter*

C. Implementation System

An implementation system will be established for the LEMTRADA REMS Program to monitor and evaluate whether the elements to assure safe use are meeting the program's goals.

a. Genzyme will ensure that LEMTRADA is only distributed to certified pharmacies and certified infusion sites by:

   i. Ensuring that distributors who distribute LEMTRADA to certified pharmacies and certified infusion sites comply with the program requirements for distributors. In order for a distributor to distribute LEMTRADA, the distributor must:

      1) Put processes and procedures in place to verify, prior to distributing LEMTRADA, that the pharmacies and infusion sites are certified by calling the LEMTRADA REMS Program (1-855-676-6326).

      2) Train all relevant staff on the LEMTRADA REMS Program requirements.

      3) Agree to be audited to ensure that all processes and procedures are in place and are being followed for the LEMTRADA REMS Program.

      4) Agree to provide distribution data to the LEMTRADA REMS Program.

   ii. Ensuring that distributors maintain patient level distribution records of all shipments of LEMTRADA to certified pharmacies and certified infusion sites and agree to provide the data to the LEMTRADA REMS Program.

   iii. Genzyme will monitor and audit the distributors within 180 days after the distributor is authorized to ensure that all processes and procedures are in place and functioning to support the requirements of the LEMTRADA REMS Program. Corrective action will be instituted by Genzyme if noncompliance is identified.

b. Genzyme will maintain a list of pharmacies and infusion sites which are certified to dispense LEMTRADA in the LEMTRADA REMS Program. Genzyme will ensure that the pharmacies' and infusion sites' certification requirements are met and may de-certify non-compliant pharmacies and infusion sites if the requirements do not continue to be met. This list will be available by telephone (1-855-676-6326) for certified prescribers of LEMTRADA.

c. Genzyme will maintain a LEMTRADA REMS Program Call Center to support healthcare providers, pharmacies, infusion sites, and patients interfacing with the LEMTRADA REMS Program.

d. Genzyme will send monthly reminders to patients enrolled in the LEMTRADA REMS Program, reminding them of the requirement for ongoing monitoring.

e. Genzyme will ensure that all materials listed in or appended to the LEMTRADA REMS document are available through the LEMTRADA REMS Program Website (www.LemtradaREMS.com) or can be accessed by calling the REMS call center (1-855-676-6326).

f. Genzyme will monitor and audit the certified pharmacies and infusion sites within 180 days after certification and has dispensed at least one LEMTRADA prescription, to ensure that all processes and procedures are in place and functioning to support the requirements of the LEMTRADA REMS Program. Corrective action will be instituted by Genzyme if noncompliance is identified.

g. Genzyme will maintain a validated, secure database of patients who are enrolled in the LEMTRADA REMS Program.

h. Genzyme will take reasonable steps to improve implementation of and compliance with the requirements in the LEMTRADA REMS Program based on monitoring and evaluation of the LEMTRADA REMS Program.

D. Timetable for Submission of Assessments

Genzyme will submit REMS Assessments to FDA at 6 and 12 months from the date of the approval of the LEMTRADA REMS, and then annually thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Genzyme will submit each assessment so that it will be received by FDA on or before the due date.

[Month] 2014

IMPORTANT DRUG WARNING

SUBJECT: Serious risks of autoimmune conditions, infusion reactions, and malignancies with LEMTRADA™ (alemtuzumab); FDA-Required REMS Program

IMPORTANT SAFETY NOTICE

Dear Healthcare Provider:

The purpose of this letter is to inform you of the approval of LEMTRADA (alemtuzumab); a CD52-directed cytolytic monoclonal antibody for intravenous infusion indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

The LEMTRADA REMS Program was developed by Genzyme in collaboration with the FDA to ensure that the benefits of LEMTRADA outweigh the serious risks. Under the LEMTRADA REMS Program, only prescribers, pharmacies, healthcare facilities, and patients enrolled in the Program are able to prescribe, dispense, administer, and receive LEMTRADA.

SERIOUS RISKS OF LEMTRADA

AUTOIMMUNE CONDITIONS

- LEMTRADA causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease. Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine cell counts at periodic intervals for 48 months after the last dose of LEMTRADA.

INFUSION REACTIONS

- LEMTRADA causes serious and life threatening infusion reactions. LEMTRADA can only be administered in certified healthcare settings that have on-site access to equipment and personnel trained to manage infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).

MALIGNANCIES

- LEMTRADA may cause an increased risk of malignancy including thyroid cancer, melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams to monitor for signs of melanoma.

LEMTRADA™ alemtuzumab 12mg IV

IMPORTANT SAFETY INFORMATION ON KNOWN RISKS

Treatment with LEMTRADA can result in the formation of autoantibodies and increase the risk of serious autoimmune mediated conditions, including ITP, other cytopenias, thyroid disorders and glomerular nephropathies, which may occur many years after treatment. In order to identify these risks, laboratory tests are required. Complete blood counts with differential, serum creatinine levels and urinalysis with urine cell counts should be obtained prior to initiation of treatment and at monthly intervals until 48 months after the last infusion with LEMTRADA. Thyroid function tests should be obtained prior to initiation of treatment and every 3 months until 48 months after the last infusion with LEMTRADA. Monitoring may need to continue past 48 months based on clinical findings of autoimmune conditions.

Most patients treated with LEMTRADA in controlled clinical trials in MS experienced infusion reactions during or after LEMTRADA administration. Some infusion reactions may be serious and life threatening. Serious reactions occurred in 3% of patients and included anaphylaxis in 2 patients (including anaphylactic shock), angioedema, bronchospasm, hypotension, chest pain, bradycardia, tachycardia (including atrial fibrillation), transient neurologic symptoms, hypertension, headache, pyrexia and rash. Premedicate patients with high dose corticosteroids (1000 mg methylprednisolone or equivalent) immediately prior to the LEMTRADA infusion and for the first 3 days of any treatment course. Observe patients for infusion reactions during and for at least 2 hours after each LEMTRADA infusion. Longer periods of observation may be required if clinically indicated.

LEMTRADA may cause an increased risk of malignancy including thyroid cancer, melanoma, and lymphoproliferative disorders. Baseline and yearly skin examinations should be performed in LEMTRADA patients to monitor for signs of melanoma. Caution should be exercised in initiating LEMTRADA therapy in patients with pre-existing or ongoing malignancies.

The LEMTRADA REMS Program Requirements:

- **Prescribers** must be enrolled in the LEMTRADA REMS Program to be able to prescribe LEMTRADA.
- **Healthcare Facilities and Pharmacies** must be enrolled in the LEMTRADA REMS Program to be able to dispense and/or administer LEMTRADA.
- **Patients** must be enrolled and authorized in the LEMTRADA REMS Program in order to receive LEMTRADA.

LEMTRADA™
alemtuzumab 12mg IV

Reporting Adverse Events

It is important that you promptly report all suspected adverse events with the use of LEMTRADA. Please contact Genzyme at 1-800-745-4447 (option 2) or the FDA at 1-800-FDA-1088 (1-800-332-1088) or www.fda.gov/medwatch.

This letter is not a comprehensive description of the risks associated with the use of LEMTRADA. Please see the enclosed Prescribing Information for a complete description of these risks.

If you have any questions about the LEMTRADA REMS Program, please call 1-855-676-6326 for more information or visit www.LemtradaREMS.com.

Sincerely,

(Name)
(Title)
Genzyme Corporation

Enclosures: LEMTRADA Prescribing Information

genzyme
A SANOFI COMPANY | www.genzyme.com

LEMTRADA™
alemtuzumab 12mg IV

For Healthcare Facilities to Complete

LEMTRADA™ alemtuzumab 12mg IV

LEMTRADA REMS HEALTHCARE FACILITY ENROLLMENT FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

LEMTRADA™ (alemtuzumab) is only available through the LEMTRADA REMS Program, a restricted distribution program. Only prescribers, pharmacies, healthcare facilities, and patients enrolled in the program are able to prescribe, dispense, administer, and receive LEMTRADA. An authorized representative of the healthcare facility must enroll the facility in the LEMTRADA REMS Program.

☐ New Enrollment
☐ Re-enrollment (every 2 years)

*Indicates a mandatory field.

Please complete a separate Healthcare Facility Enrollment Form for each facility site, if applicable.

HEALTHCARE FACILITY INFORMATION (Please Print)

Name of Institution or Healthcare Facility*		NPI Number*	
Infusion Facility Address*			
City*		State*	ZIP Code*
Ship-to Street Address (if different)*			
City*		State*	ZIP Code*
Phone Number*	Fax Number*	Email Address	
Name of Authorized Healthcare Facility Representative*		Title*	

Site Affiliation

☐ Academic ☐ Government ☐ Ambulatory/Free Standing ☐ Hospital Based ☐ Private Practice (in office)

HEALTHCARE FACILITY AGREEMENT

I am the Authorized Representative designated by my healthcare facility to coordinate the activities of the LEMTRADA REMS Program. By signing this form, I agree to comply with the following program requirements:

- I understand that my healthcare facility must be certified with the LEMTRADA REMS Program to receive or administer LEMTRADA.
- I have completed the *LEMTRADA REMS Education Program for Healthcare Facilities*.
- I understand the risk of serious infusion reactions during and following the administration of LEMTRADA.
- I understand the need to monitor patients for infusion reactions during and for at least 2 hours after each LEMTRADA infusion.
  - To include the monitoring of patient vital signs before the infusion and periodically during the infusion.
- I understand that my healthcare facility must be equipped with the necessary on-site equipment and personnel to manage anaphylaxis or serious infusion reactions.
- I understand that my healthcare facility must renew enrollment in the LEMTRADA REMS Program every 2 years from initial enrollment.

Reference ID: 3658409

genzyme
A SANOFI COMPANY

HEALTHCARE FACILITY AGREEMENT (CONTINUED)

- This healthcare facility will establish procedures and protocols that are subject to audit, to help ensure compliance with the safe use conditions required in the LEMTRADA REMS Program, including the following:
  - Ensuring a *LEMTRADA REMS Patient Authorization and Baseline Lab Form* is received for each prescription by contacting the LEMTRADA REMS Program.
  - All non-prescribing HCPs who administer LEMTRADA in my healthcare setting are trained using the *LEMTRADA REMS Program Overview* and the *LEMTRADA REMS Education Program for Healthcare Facilities* and a record regarding such training must be maintained.
  - Prior to the first day of each treatment course, counsel and provide a copy of *What You Need To Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide* to each patient to inform them about the risk of serious infusion reactions.
  - Observe each patient administered LEMTRADA at my healthcare facility during and for at least 2 hours after each LEMTRADA infusion, in order to provide appropriate medical treatment in the event of serious infusion reactions following LEMTRADA infusion.
- This healthcare facility must ensure that LEMTRADA is not dispensed outside of the authorized representative's certified healthcare facility.
- To make available to Genzyme, documentation to verify understanding of, and adherence to, the requirements of the LEMTRADA REMS Program.
- For each patient, complete and return the *LEMTRADA REMS Infusion Checklist* to the LEMTRADA REMS Program within 5 business days from the patient's last infusion of LEMTRADA within a specific treatment course.
- To return to Genzyme, any unused vials of LEMTRADA within 50 days from the date of receipt of the *Lemtrada REMS Patient Authorization and Baseline Lab Form*.

Authorized Healthcare Facility Representative Signature* Date*

Print Name* Title

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

Reference ID: 3658409

genzyme
A SANOFI COMPANY

For Prescribers to Complete

LEMTRADA™ alemtuzumab 12mg IV

LEMTRADA REMS PATIENT STATUS FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

This form must be completed every 6 months for each LEMTRADA patient under your care. Please complete this form 6 months after your patient's first infusion with LEMTRADA and every 6 months thereafter, until 48 months after the patient's last infusion.

*Indicates a mandatory field.

PRESCRIBER INFORMATION (PLEASE PRINT)

Name (first, last)*	Office Phone Number*	
Address*		
City*	State*	ZIP Code*

PATIENT INFORMATION (PLEASE PRINT)

Name (first, last)*

Patient LEMTRADA REMS Program Identification Number*

Date of Birth (MM/DD/YYYY)*	Date of Last LEMTRADA Infusion (MM/DD/YYYY)*

Is the above-named patient still under your care?* (Check one) ☐ **Yes** ☐ **No**

If NO, please indicate the name of the healthcare provider now responsible for this patient's care.

Healthcare Provider Name

Healthcare Provider Phone Number

Patient's Current Healthcare Provider is Unknown ☐

IF YES, please complete the following information

The patient has completed the periodic monitoring within the last 6 months. ☐ Yes ☐ No

Since submitting the last LEMTRADA REMS Patient Status Form, has the patient been diagnosed with any of the following?

a. Autoimmune Conditions ☐ Yes ☐ No

b. Infusion reactions ☐ Yes ☐ No

c. Malignancies ☐ Yes ☐ No

☐ This adverse event has already been reported to Genzyme (specify date of report):

Report all adverse events to Genzyme Medical Information at 1-800-745-4447 (option 2) or the FDA at 1-800-FDA -1088 (1-800-332-1088) or www.FDA.gov/medwatch

In signing this form, I acknowledge that I have reviewed *What You Need to Know About LEMTRADA Treatment: A Patient Guide* with this patient and counseled the patient about the serious risks associated with the use of LEMTRADA, and how to mitigate these risks through periodic monitoring.

Prescriber's Signature

Prescriber Signature* Date*

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

genzyme A SANOFI COMPANY

LEMTRADA REMS Program Overview

What is the LEMTRADA REMS (Risk Evaluation and Mitigation Strategy) Program?

A REMS is a strategy to manage known or potential risks associated with a drug, and is required by the FDA to ensure that the benefits of the drug outweigh its risks. Due to serious risks of autoimmune conditions, infusion reactions and malignancies, LEMTRADA is only available through a restricted program called the LEMTRADA REMS Program.

LEMTRADA REMS Program Requirements

- **Prescribers** must be enrolled in the LEMTRADA REMS Program to be able to prescribe LEMTRADA.
- **Healthcare facilities and Pharmacies** must be enrolled in the LEMTRADA REMS Program to be able to dispense and/or administer LEMTRADA.
- **Patients** must be enrolled and authorized in the LEMTRADA REMS Program in order to receive LEMTRADA.

PRESCRIBER ENROLLMENT INSTRUCTIONS

1. Complete the training program, which includes reviewing the following:
   - LEMTRADA REMS Prescribing Information
   - LEMTRADA REMS Program Overview
   - LEMTRADA Education Program for Prescribers
2. Successfully complete the 8-question LEMTRADA REMS Knowledge Assessment.
3. Enroll in the program by completing a LEMTRADA REMS Prescriber Enrollment Form.
4. Submit the completed and signed Forms to the LEMTRADA REMS Program.

PATIENT ENROLLMENT INSTRUCTIONS

1. Complete the LEMTRADA REMS Patient Enrollment Form which contains information to be completed by both the prescriber and the patient.
2. Provide a copy of What You Need to Know About LEMTRADA Treatment: A Patient Guide and a LEMTRADA Patient Safety Information Card to each patient who will receive LEMTRADA. You must use What You Need to Know About LEMTRADA Treatment: A Patient Guide to counsel your patients on the serious risks and REMS requirements with the use of LEMTRADA.
3. Submit the completed and signed LEMTRADA REMS Patient Enrollment Form to the LEMTRADA REMS Program.
4. Provide the patient a copy of the LEMTRADA REMS Patient Enrollment Form and keep a copy in the patient's medical record.

LEMTRADA™ alemtuzumab 12mg IV

(continued on next page)

HEALTHCARE FACILITY ENROLLMENT INSTRUCTIONS

1. An authorized representative must enroll on behalf of the healthcare facility by reviewing the LEMTRADA REMS Education Program for Healthcare Facilities and completing the LEMTRADA REMS Healthcare Facility Enrollment Form, which acknowledges that the healthcare facility agrees to follow the procedures outlined in the LEMTRADA REMS Program, including:
   - All staff at the facility who will be involved with the dispensing and administration of LEMTRADA must be trained.
   - The healthcare facility will verify that prescribers are certified and patients are authorized to receive LEMTRADA prior to dispensing or administering LEMTRADA.
   - The healthcare facility will provide a copy of What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide to the patient on the first day of each treatment course when LEMTRADA is dispensed.
   - The healthcare facility will complete a LEMTRADA REMS Infusion Checklist for each patient at the conclusion of each treatment course and submit the LEMTRADA REMS Program within 5 business days.
   - Enrollment in the LEMTRADA REMS Program must be renewed every 2 years from initial enrollment.

2. Submit the completed and signed LEMTRADA REMS Healthcare Facility Enrollment Form to the LEMTRADA REMS Program.

PHARMACY ENROLLMENT INSTRUCTIONS

1. An authorized representative must enroll on behalf of the Pharmacy by reviewing the LEMTRADA REMS Program Overview and completing the LEMTRADA REMS Pharmacy Enrollment Form, which acknowledges that the Pharmacy agrees to follow the procedures outlined in the LEMTRADA REMS Program, including:
   - All relevant staff at the Pharmacy who will be involved with the dispensing of LEMTRADA must be educated and trained.
   - The Pharmacy will verify that a LEMTRADA REMS Prescription Ordering Form is received for each prescription.
   - The Pharmacy will verifty that prescribers and healthcare facilities are certified and patients are authorized to receive LEMTRADA prior to dispensing LEMTRADA.
   - Enrollment in the LEMTRADA REMS Program must be renewed every 2 years from initial enrollment.

2. Submit the completed and signed LEMTRADA REMS Pharmacy Enrollment Form to the LEMTRADA REMS Program.

Where to find REMS Program Information and Resources

To enroll in the LEMTRADA REMS Program call 1-855-676-6326. For information related to enrollment in the LEMTRADA REMS Program, call 1-855-676-6326 or visit www.LEMTRADAREMS.com.

Indication

LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

The Prescribing Information includes a **BOXED WARNING** for LEMTRADA:

Please see accompanying Prescribing Information for complete safety information, including BOXED WARNING.

genzyme A SANOFI COMPANY | www.genzyme.com

LEMTRADA™ alemtuzumab 12mg IV

For Prescribers to Complete

LEMTRADA™ alemtuzumab 12mg IV

LEMTRADA REMS PRESCRIBER ENROLLMENT FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

LEMTRADA™ (alemtuzumab) is available only through the LEMTRADA REMS Program, a restricted distribution program. Only prescribers, pharmacies, healthcare facilities, and patients enrolled in the program are able to prescribe, dispense, administer, and receive LEMTRADA.

Instructions:

1. Review the LEMTRADA REMS Education Program for Healthcare Providers, including the Prescribing Information
2. Successfully complete the LEMTRADA REMS Knowledge Assessment
3. Complete and submit this LEMTRADA REMS Prescriber Enrollment Form
4. Send your patient to a healthcare facility that is enrolled in LEMTRADA REMS program

Please complete all required fields on the next pages and fax the pages to 1-855-557-2478. You will receive enrollment confirmation via your preferred method of communication (email or fax) within 2 business days.

*Indicates a mandatory field.

LEMTRADA PRESCRIBER INFORMATION (PLEASE PRINT)

Name (first, last)/Degree*

Name of Institution or Healthcare Facility*

City*	State*	ZIP Code*

Office Phone Number*	Fax Number*	Email Address	Mobile Phone Number

National Provider Identification (NPI) Number*

If you are dispensing LEMTRADA from your clinic, a LEMTRADA REMS Healthcare Facility Enrollment Form must also be completed and submitted.

PRESCRIBER AGREEMENT

By completing this form, I attest that:

- I understand that LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.
- I understand that LEMTRADA is only available through the LEMTRADA REMS Program and that I must comply with the program requirements in order to prescribe LEMTRADA.
- I have completed the *LEMTRADA REMS Education Program for Prescribers*, including review of the LEMTRADA Prescribing Information, and successfully completed the *LEMTRADA REMS Knowledge Assessment*.
- I understand that by completing the training program and signing this *LEMTRADA REMS Prescriber Enrollment Form*, I will be enrolled in the LEMTRADA REMS Program and can prescribe LEMTRADA.
- I understand that I am responsible for reviewing *What You Need to Know About LEMTRADA Treatment: A Patient Guide* with each patient, and counseling each patient on an ongoing basis about the serious risks associated with the use of LEMTRADA and how to mitigate these risks through periodic monitoring.
- I understand that I must enroll all patients being treated with LEMTRADA into the LEMTRADA REMS Program prior to initiating the patient on treatment with LEMTRADA. I am responsible for completing a *LEMTRADA REMS Patient Enrollment Form* with the patient (or patient's legal representative), obtaining the patient's (or patient's legal representative's) signature on the form, and submitting the signed form to the LEMTRADA REMS Program. A completed copy should be provided to the patient and another copy should be stored in the patient's records.
- I will provide enrolled patients with a *LEMTRADA Patient Safety Information Card* and instruct patients to carry this card with them at all times in case of an emergency.
- I understand that I must submit a *LEMTRADA REMS Prescription Ordering Form* for each LEMTRADA prescription. I understand that I am responsible for completing baseline lab monitoring within 30 days prior to infusion of LEMTRADA.

genzyme
A SANOFI COMPANY

PRESCRIBER AGREEMENT (CONTINUED)

- I understand that I must submit a *LEMTRADA REMS Patient Authorization and Baseline Lab Form* indicating completion of each patient's baseline labs within 30 days prior to the patient's infusion date.
- I understand the risks of autoimmune conditions and malignancies associated with the use of LEMTRADA, and the need for periodic monitoring in order to identify and mitigate these risks:
  - Complete blood counts with differential obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Serum creatinine levels obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Urinalysis with urine cell counts obtained within 30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the last infusion.
  - Thyroid function tests, such as thyroid stimulating hormone (TSH) level, obtained within 30 days prior to initiation of treatment and every 3 months thereafter until 48 months after the last infusion.
  - Baseline and yearly skin examinations.
- I will report any adverse events of autoimmune conditions, infusion reactions, or malignancies to Genzyme.
- I will complete the *LEMTRADA REMS Patient Status Form* 6 months after the patient's first infusion and every 6 months thereafter, until 48 months after the completion of the patient's last infusion.
- I understand that I will notify Genzyme if a patient is no longer under my care.
- I understand that if I fail to comply with the requirements of the LEMTRADA REMS Program, I may no longer be able to participate in the Program.
- I understand Genzyme and its agents may contact me via phone, mail, fax, or email to support administration of the LEMTRADA REMS Program.

Prescriber Signature* Date*

Print Name*

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

Reference ID: 3658409

genzyme
A SANOFI COMPANY

For Healthcare Facilities to Complete

LEMTRADA™ alemtuzumab 12mg IV

LEMTRADA REMS INFUSION CHECKLIST

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

As a condition of your healthcare facility's authorization to infuse LEMTRADA, this Infusion Checklist **must** be completed for each patient by the last day of each patient's treatment course and faxed within **5 business days**. **This Infusion Checklist must also be completed and returned even if LEMTRADA is not infused**. Keep a copy of this checklist in the patient's medical record.

All fields on this form are mandatory.

PATIENT INFORMATION (PLEASE PRINT)

Patient Name (first, last) | DOB (MM/DD/YYYY)

Patient LEMTRADA REMS Program Identification Number

PRESCRIBER INFORMATION (PLEASE PRINT)

Prescriber Name (first, last)

Prescriber LEMTRADA REMS Program Identification Number

HEALTHCARE FACILITY INFORMATION (PLEASE PRINT)

Healthcare Facility Name

Healthcare Facility LEMTRADA REMS Program Identification Number

STEP 1: CONFIRM that the patient is authorized to receive LEMTRADA

You must contact the LEMTRADA REMS Program by phone (1-855-676-6326) prior to initiation of each treatment course.

Is the patient authorized to receive LEMTRADA? ☐ **Yes** ☐ **No**

Yes Continue to next question

No STOP — DO NOT INFUSE. Refer patient back to the LEMTRADA prescriber.

STEP 2: CONFIRM that the patient has been counseled and has received "What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide."

The patient must be counseled about the risk for infusion reactions and provided with "What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide" prior to the first infusion of each treatment course. Has the patient been counseled and received the Guide?

☐ **Yes** ☐ **No**

Yes Continue to next question

No STOP — provide the Patient Guide. Proceed to the next question after the patient has received this Guide and has been counseled.

STEP 3: CONFIRM appropriate medical measures available for infusion

Appropriate medical support measures are available:

1. In case of serious infusion reactions.
2. To monitor patient's vital signs during and post-infusion.

Are the appropriate medical measures listed above available? ☐ **Yes** ☐ **No**

Yes Continue to next question

No **STOP — DO NOT INFUSE** until appropriate medical support measures are available. Please contact the LEMTRADA REMS Program for additional information .

(continued on the back)

STEP 4: Record infusion information

Was patient infused with LEMTRADA? ☐ **Yes** ☐ **No**

Yes Fill in Dates of Infusion below and then proceed to Step 5

No Proceed to Step 5.

LEMTRADA Infusions

Dates of Infusion:

Date: _____ Date: _____

Date: _____ Date: _____

Date: _____

STEP 5: Return of Unused Vials of LEMTRADA

Unused vials of LEMTRADA must be returned within 50 days of submission of the LEMTRADA REMS Patient Authorization and Baseline Lab Form. Contact the LEMTRADA REMS Program at 1-855-676-3626 for additional information.

_____ _____

Signature of staff completing checklist Date

_____

Name of staff completing checklist (Please Print)

Report all adverse events to Genzyme Medical Information at 1-800-745-4447 (option 2) or the FDA at 1-800-FDA-1088 (1-800-332-1088) or www.FDA.gov/medwatch.

STEP 6: Fax the Infusion Checklist to the LEMTRADA REMS Program at 1-855-557-2478

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326.

genzyme
A SANOFI COMPANY

For Patients to Complete

LEMTRADA™ alemtuzumab 12mg IV

LEMTRADA REMS PATIENT ENROLLMENT FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

This form must be completed before you can receive LEMTRADA™ (alemtuzumab). LEMTRADA is available only through a restricted distribution program called the LEMTRADA REMS Program. Your prescriber will help you complete this form and will give you a copy.

*Indicates a mandatory field.

PATIENT INFORMATION (PLEASE PRINT)

Name (first, last)*	Date of Birth (MM/DD/YYYY)*		
Street Address*	City*	State*	ZIP Code*
Phone Number*	Gender* ☐ Male ☐ Female		
Secondary Contact (first, last)	Phone Number		

PRESCRIBER INFORMATION (PLEASE PRINT)

Prescriber Name (first, last)*	NPI Number*	Phone Number*

PATIENT AGREEMENT

By signing this form, I acknowledge that:

- I have received, read, and understand *What You Need to Know about LEMTRADA Treatment: A Patient Guide* that my doctor has given to me.
- My doctor has reviewed with me the benefits and risks of treatment with LEMTRADA.
- I am aware that LEMTRADA is associated with serious risks, including autoimmune conditions, infusion reactions and malignancies, and that these complications can be identified through periodic monitoring and awareness of the initial signs and symptoms.
- I understand the need to have blood and urine tests within 30 days prior to my first LEMTRADA treatment, then each month for 4 years following my last treatment with LEMTRADA.
- I understand the need to have thyroid testing within 30 days prior to my first LEMTRADA treatment, then every 3 months for 4 years following my last treatment with LEMTRADA.
- I understand the need to have yearly skin exams from my first LEMTRADA treatment, and continuing for 4 years following my last treatment with LEMTRADA.
- I will tell my doctor if I have any reactions or symptoms after receiving LEMTRADA.
- I understand that I must tell all my doctors that I have received LEMTRADA.
- I understand that in order to receive LEMTRADA, I am required to enroll in the LEMTRADA REMS Program and my information will be stored in a secure and confidential database of all patients who receive LEMTRADA in the United States. After enrolling, my doctor will provide me with a signed copy of the enrollment form.
- My doctor has counseled and provided me with a *LEMTRADA Patient Safety Information Card* which I should carry with me at all times in case of an emergency.
- I understand that I must tell Genzyme if I change my doctor.
- I understand that I must tell Genzyme if my contact information changes.
- I give permission to Genzyme and its agents to use and share my personal health information for the purposes of enrolling me into the LEMTRADA REMS Program, coordinating the dispensing of receiving LEMTRADA, administering the LEMTRADA REMS Program, and releasing my personal health information to the Food and Drug Administration (FDA) as necessary.
- By completing the information below, I understand Genzyme and its agents will contact me via phone, mail or email to support administration of the LEMTRADA REMS Program.

I prefer to be contacted:
By mail ☐
By phone ☐
By email (please provide email address) ☐_____

Patient/Legal Representative Signature* | Relationship to Patient*

Print Name* | Date*

I acknowledge that I have explained the LEMTRADA REMS Program to this patient.

Prescriber Signature* | Date*

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

Reference ID: 3658409

genzyme A SANOFI COMPANY

LEMTRADA™

alemtuzumab 12mg IV

Patient Safety Information Card

Please show this card to all emergency workers and healthcare providers.

Important information to know about LEMTRADA

<<insert your name>>

has been treated with LEMTRADA, a treatment for multiple sclerosis (MS) which lowers the number of circulating white blood cells for a period of time after treatment and also affects the immune system. Therefore, the patient is part of a laboratory monitoring program that continues for 4 years after his/her last treatment.

Reference ID: 3658409

LEMTRADA™
alemtuzumab

LEMTRADA treatment can increase the risk of:

Autoimmune conditions such as:

- A bleeding problem called immune thrombocytopenia (ITP)
- Other blood disorders (including neutropenia, hemolytic anemia, and pancytopenia)
- Disorders of the thyroid gland (hypo/hyperthyroidism)
- Kidney disorders (nephropathies, including anti-glomerular basement membrane [anti-GBM] disease)

Reference ID: 3658409

Infusion reactions (may occur more than 24 hours after the infusions), such as:

- Hypersensitivity reactions (including anaphylaxis)
- Fever
- Hives
- Irregular heartbeat
- Nausea
- Chest pain
- Low blood pressure

Malignancies such as:

- Thyroid Cancer
- Melanoma
- Lymphoproliferative disorders and lymphoma

	Healthcare Provider's name (eg, neurologist)	Healthcare Provider's name (eg, primary care provider)
Name:		
Phone Number:		
Fax Number: (for medical records or lab tests)		

For more information on LEMTRADA, including important risks, please refer to the Prescribing Information and/or www.LEMTRADA.com.

For information on LEMTRADA or the LEMTRADA REMS Program, call 1-855-676-6326.

genzyme
A SANOFI COMPANY

LEMTRADA™
alemtuzumab 12 mg IV

Reference ID: 3658409

LEMTRADA REMS (Risk Evaluation and Mitigation Strategy) Program

What is the LEMTRADA REMS Program?

A REMS is a strategy to manage known or potential serious risks associated with a drug product and is required by the FDA to ensure the benefits of a drug outweigh its risks. The purpose of the LEMTRADA REMS Program is to inform prescribers, pharmacies, healthcare facilities, and patients about the risks of:

AUTOIMMUNE CONDITIONS

LEMTRADA™ (alemtuzumab) causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease. Monitor complete blood counts with differential, serum creatinine levels, and urinalysis with urine cell counts at periodic intervals for 48 months after the last dose of LEMTRADA.

INFUSION REACTIONS

LEMTRADA causes serious and life threatening infusion reactions. LEMTRADA must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions.

MALIGNANCIES

LEMTRADA may cause an increased risk of malignancies including thyroid cancer, melanoma, and lymphoproliferative disorders. Perform baseline and yearly skin exams.

FOLD

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326

LEMTRADA REMS Program Requirements

PRESCRIBERS

Prescribers must be enrolled in the LEMTRADA REMS Program to prescribe LEMTRADA for patients with multiple sclerosis.

Learn about Prescriber Enrollment ▸

HEALTHCARE FACILITIES

Healthcare facilities must be enrolled in the LEMTRADA REMS Program to dispense/administer LEMTRADA for patients with multiple sclerosis. *One representative needs to enroll per healthcare setting.*

Learn about Healthcare Facility Enrollment ▸

PHARMACIES

Pharmacies must be enrolled in the LEMTRADA REMS Program to be able to dispense LEMTRADA for patients with multiple sclerosis.

Learn about Pharmacy Enrollment ▸

LEMTRADA REMS Program Prescriber Enrollment

- Prescribers must be enrolled in the LEMTRADA REMS Program to be able to prescribe LEMTRADA™ (alemtuzumab) for patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS
- Note that your healthcare facility must be separately enrolled in the LEMTRADA REMS Program to dispense/administer LEMTRADA

To enroll in the Program, prescribers must complete the following steps:

1	**Review** the LEMTRADA REMS Education Program for Prescribers, including the LEMTRADA REMS Program Overview and the LEMTRADA Prescribing Information
2	**Successfully complete** the 8-question Knowledge Assessment
3	**Complete and sign** the LEMTRADA REMS Prescriber Enrollment Form

FOLD

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326

PROGRAM MATERIALS

For Prescribers

- LEMTRADA REMS Program Overview
- LEMTRADA REMS Education Program for Prescribers
- LEMTRADA REMS Knowledge Assessment
- LEMTRADA REMS Patient Status Reminder Letter
- LEMTRADA REMS Prescriber Enrollment Form
- LEMTRADA REMS Patient Authorization and Baseline Lab Form
- LEMTRADA REMS Patient Enrollment Form
- LEMTRADA REMS Prescription Ordering Form
- LEMTRADA REMS Patient Status Letter
- What You Need to Know About LEMTRADA Treatment: A Patient Guide

Adobe® Reader® is required to view all of these PDFs. If you do not have it installed, download it free here.

LEMTRADA REMS Healthcare Facility Enrollment

- Healthcare facilities must be enrolled in the LEMTRADA REMS Program to be able to dispense/administer LEMTRADA™ (alemtuzumab) for patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS

To enroll in the Program, an Authorized Representative of the healthcare facility must complete the following steps:

1	**Designate** an Authorized Representative
2	**Review** the LEMTRADA REMS Education Program for Healthcare Facilities, including the Prescribing Information
3	**Complete and sign** the LEMTRADA REMS Healthcare Facility Enrollment Form. This enrollment must be renewed every 2 years
4	**Implement** the necessary staff training and processes to comply with the LEMTRADA REMS Program requirements

FOLD

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326

PROGRAM MATERIALS

For Healthcare Facilities

- LEMTRADA REMS Program Overview
- LEMTRADA REMS Education Program for Healthcare Facilities
- LEMTRADA REMS Healthcare Facility Enrollment Form
- LEMTRADA REMS Infusion Checklist
- What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide

Adobe® Reader® is required to view all of these PDFs. If you do not have it installed, download it free here.

US.MS.LEM.14.10.013-v1

genzyme A SANOFI COMPANY

LEMTRADA REMS Program Pharmacy Enrollment

- Pharmacies must be enrolled in the LEMTRADA REMS Program to be able to dispense LEMTRADA™ (alemtuzumab) for patients with multiple sclerosis

To enroll in the Program, an Authorized Representative of the pharmacy must complete the following steps:

1	**Designate** an Authorized Representative
2	**Review** the LEMTRADA REMS Overview
3	**Complete and sign** the LEMTRADA REMS Pharmacy Enrollment Form. This enrollment form must be renewed every 2 years
4	**Implement** the necessary staff training and processes to comply with the LEMTRADA REMS Program requirements

PROGRAM MATERIALS

For Pharmacies

- LEMTRADA REMS Program Overview
- LEMTRADA REMS Pharmacy Enrollment Form

Adobe® Reader® is required to view all of these PDFs. If you do not have it installed, download it free here.

FOLD

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326

LEMTRADA Patient Guides

Below are materials that help inform patients about treatment with LEMTRADA.

- What You Need to Know About LEMTRADA Treatment: A Patient Guide
- What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide

Adobe® Reader® is required to view all of these PDFs. If you do not have it installed, download it free here.

FOLD

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326

LEMTRADA REMS Program Enrollment Forms and Resources

Below are downloadable forms needed to support the LEMTRADA REMS Program.

MATERIALS FOR PRESCRIBERS

- LEMTRADA REMS Program Overview
- LEMTRADA REMS Education Program for Prescribers
- LEMTRADA REMS Knowledge Assessment
- LEMTRADA REMS Patient Status Reminder Letter
- LEMTRADA REMS Prescriber Enrollment Form
- LEMTRADA REMS Patient Authorization and Baseline Lab Form
- LEMTRADA REMS Patient Enrollment Form
- LEMTRADA REMS Prescription Ordering Form
- LEMTRADA REMS Patient Status Letter
- What You Need to Know About LEMTRADA Treatment: A Patient Guide

FOLD

MATERIALS FOR HEALTHCARE FACILITIES

- LEMTRADA REMS Program Overview
- LEMTRADA REMS Education Program for Healthcare Facilities
- LEMTRADA REMS Healthcare Facility Enrollment Form
- LEMTRADA REMS Infusion Checklist
- What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide

MATERIALS FOR PHARMACIES

- LEMTRADA REMS Program Overview
- LEMTRADA REMS Pharmacy Enrollment Form

Adobe® Reader® is required to view all of these PDFs. If you do not have it installed, download it free here.

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326

Reference ID: 3658409

Contact Us

For questions about the LEMTRADA REMS Program, please contact us by phone at 1-855-676-6326 or complete the form below.

All fields are required.

First Name

Last Name

What can we help you with?

How would you like to be contacted?

Email Phone

FOLD

Email Address

Submit

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326

Contact Us

For questions about the LEMTRADA REMS Program, please contact us by phone at 1-855-676-6326 or complete the form below.

All fields are required.

First Name

Last Name

What can we help you with?

How would you like to be contacted?

Email Phone

FOLD

Phone Number

Submit

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326

LEMTRADA™ alemtuzumab

Important Safety Information | Prescribing Information | Medication Guide

Home | Prescriber Enrollment | Healthcare Facility Enrollment | Pharmacy Enrollment | Patient Guides | Forms & Resources

Contact Us

For questions about the LEMTRADA REMS Program, please contact us by phone at 1-855-676-6326 or complete the form below.

All fields are required.

First Name

Last Name

What can we help you with?

- Patient Support
- Product
- Technical
- Other

FOLD

Submit

If you have questions about the LEMTRADA REMS Program or need help enrolling, call 1-855-676-6326

This site is intended for United States residents only.

US.MS.LEM.14.10.013-v1

genzyme A SANOFI COMPANY

Thank You

Thank you for contacting us. Please remember that the information you provided will be kept strictly confidential and will not be shared with other parties. You will be contacted by a Genzyme representative to address your concern. If your issue is not resolved in a timely manner, please call us at 1-855-676-6326.

FOLD

For Patients

What You Need to Know About LEMTRADA Treatment and Infusion Reactions: A Patient Guide

LEMTRADA™ (alemtuzumab) Infusion Reactions: What You Need to Know

- Infusion reactions, are side effects linked to the infusion of LEMTRADA. LEMTRADA can cause serious infusion reactions that may cause death. Serious infusion reactions may happen while you receive, or up to 24 hours or longer after you receive LEMTRADA.
- Most patients treated with LEMTRADA will experience side-effects at the time of the infusion.
- The most common infusion reactions for patients who receive LEMTRADA were nausea, hives, itching, difficulty sleeping, chills, flushing, fatigue, shortness of breath, congestion of the lungs, upset stomach, dizziness and pain.
- Some serious reactions are possible, such as life-threatening allergic reactions, swelling, wheezing, low blood pressure, chest pain, a fast, slow, or irregular heartbeat, transient neurologic symptoms, high blood pressure, headache, fever, and rash.
- A serious allergic reaction called anaphylaxis, which can cause death if not properly treated, was reported rarely.

LEMTRADA can only be given at a certified healthcare facility that has the necessary equipment and personnel to manage infusions reactions.

Steps you and your healthcare provider can take to help manage infusion reactions

- The healthcare facility where you receive LEMTRADA has personnel who are trained and medical equipment needed to treat infusion reactions.
- Your healthcare provider will give you medication called a corticosteroid, and possibly other medications—such as anti-allergy medications (antihistamines) and anti-fever medications (antipyretics), to help avoid infusion reactions or make them milder. Corticosteroids are usually given through a vein in your arm on the first 3 days of your infusions, just before your LEMTRADA infusion.

LEMTRADA™
alemtuzumab 12mg IV

- You will be closely monitored during the infusion and for at least 2 hours following the completion of the infusion to watch for any infusion reactions. Your healthcare provider may continue to monitor you for longer if needed.
- Should an infusion reaction occur, your healthcare provider will likely provide treatment, as needed.
  - Medication may be given for relief of your symptoms. For example, antihistamines may help relieve an itchy rash.
  - Infusions usually take about 4 hours; however, your healthcare provider may slow down the infusion or stop it temporarily.
  - If an infusion is stopped, your healthcare provider might try to administer LEMTRADA again, but more slowly and with additional medicine to try to stop an infusion reaction from happening again.
  - If your healthcare provider suspects you might be having a serious allergic reaction, the LEMTRADA infusion will be stopped, and you may receive medication or other measures to treat this reaction. In addition to medication, IV fluids may be given.

Make sure to speak up

If you experience any discomfort or anything that feels out of the ordinary during your infusion, be sure to immediately tell the healthcare provider providing the infusion. If symptoms occur after you have left the healthcare facility, be sure to notify your doctor as soon as possible.

Tell your healthcare provider right away if you have any of the following symptoms of a serious infusion reaction during the infusion or after you have left the healthcare facility:

- swelling in your mouth or throat
- trouble breathing
- weakness
- fast, slow, or irregular heart beat
- chest pain
- rash

US.MS.LEM.14.10.015-v1

LEMTRADA™ alemtuzumab 12mg IV

LEMTRADA REMS Education Program for Healthcare Facilities

This Educational Piece Includes Information About:

- The LEMTRADA REMS Program requirements to implement in your healthcare facility
- Serious risks of autoimmune conditions, infusion reactions, and malignancies
- Proper administration of LEMTRADA

The LEMTRADA REMS Education Program for Prescribers Includes Additional Information About:

- Steps for PRESCRIBER enrollment
- Ordering of LEMTRADA
- Patient Counseling

LEMTRADA™
alemtuzumab 12mg IV

What is the LEMTRADA REMS (Risk Evaluation and Mitigation Strategy) Program?

A REMS Program is a strategy to manage known or potential risks associated with a drug, and is required by FDA to ensure that the benefits of the drug outweigh its risks. LEMTRADA is only available under a restricted program called the LEMTRADA REMS Program because of the risks of infusion reactions, autoimmune conditions, and malignancies. The LEMTRADA REMS Education Program for Healthcare Facilities is designed to educate and train healthcare facilities' Authorized Representatives on the serious risks associated with LEMTRADA, the LEMTRADA REMS Program requirements and how to properly administer LEMTRADA.

- **Prescribers** must be enrolled in the LEMTRADA REMS Program to be able to prescribe LEMTRADA.
- **Healthcare facilities and pharmacies** must be enrolled in the LEMTRADA REMS Program to be able to dispense /administer LEMTRADA.
- **Patients** must be enrolled and authorized in the LEMTRADA REMS Program in order to receive LEMTRADA.

Steps for Healthcare Facility Certification

1	Designate an Authorized Representative
2	Review the LEMTRADA REMS Education Program for Healthcare Facilities, including the Prescribing Information
3	Complete and sign the LEMTRADA REMS Healthcare Facility Enrollment Form. This Enrollment must be renewed every 2 years.
4	Implement the necessary staff training and processes to comply with the LEMTRADA REMS Program requirements.

The LEMTRADA REMS Education Program for Certified Healthcare Facilities, LEMTRADA REMS Healthcare Facility Enrollment Form, and other LEMTRADA REMS Program tools are available online at www.LEMTRADAREMS.com or by contacting the LEMTRADA REMS Program at 1-855-676-6326.

To enroll in the LEMTRADA REMS Program call 1-855-676-6326.

Who Can Be An Authorized Representative?

An Authorized Representative at the healthcare facility can be a:

- Pharmacist
- Director of infusion center
- Prescriber
- Nurse
- Or, any responsible individual in the healthcare facility

Please check with your manager to ensure the appropriate person represents the healthcare facility and attests to the enrollment requirements as stated on the LEMTRADA REMS Healthcare Facility Enrollment Form.

- One representative needs to enroll per healthcare facility (the "Authorized Representative"). One Authorized Representative can manage more than one healthcare facility.
- Please note, there are no LEMTRADA REMS requirements for staff at a healthcare facility who will not be involved with dispensing or administering LEMTRADA.

Overview of Important Safety Information

Indication

LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

The Prescribing Information includes a **BOXED WARNING** for LEMTRADA.

Please see the Prescribing Information for complete safety information, including BOXED WARNING.

Serious Risks Associated with LEMTRADA

Infusion Reactions

Most patients treated with LEMTRADA in controlled clinical trials in MS experienced infusion reactions during or after LEMTRADA administration. In some patients, infusion reactions were reported more than 24 hours after LEMTRADA infusion. Serious reactions occurred in 3% of patients including cases of anaphylaxis in 2 patients (including anaphylactic shock), angioedema, bronchospasm, hypotension, chest pain, bradycardia, tachycardia (including atrial fibrillation), transient neurologic symptoms, hypertension, headache, pyrexia, and rash. Other infusion reactions included nausea, urticaria, pruritus, insomnia, chills, flushing, fatigue, dyspnea, pulmonary infiltrates, dysgeusia, dyspepsia, dizziness, and pain. In clinical studies, 0.6% of patients with infusion reactions received epinephrine or atropine.

Premedicate patients with high dose corticosteroids (1,000 mg of methylprednisolone or equivalent) immediately prior to LEMTRADA infusion and for the first 3 days of each treatment course. Consider pretreatment with antihistamines and/or antipyretics prior to LEMTRADA administration. Infusion reactions may occur in patients despite pretreatment.

LEMTRADA can only be administered in certified healthcare settings that have on-site access to equipment and personnel trained to manage infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).

Patients must be observed for infusion reactions during and for at least 2 hours after each LEMTRADA infusion. Consider longer periods of observation if clinically indicated. Vital signs should be monitored before and periodically during the infusion. If an infusion reaction occurs, appropriate symptomatic treatment should be provided as needed. If the infusion is not well tolerated, the duration of the infusion may be extended. If severe infusion reactions occur, immediate discontinuation of the infusion should be considered.

Autoimmune Conditions

LEMTRADA has been associated with risk of autoimmune conditions, including immune thrombocytopenia, thyroid disorders and glomerular nephropathies, which may occur many years after treatment and may be serious or life-threatening. Early detection can help to improve the outcomes of patients experiencing these events.

Please review the sections that follow to gain a better understanding of the risks of autoimmune conditions.

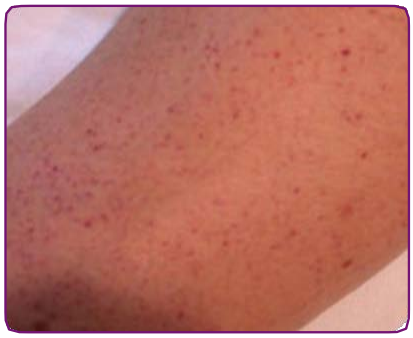
• *Immune Thrombocytopenia (ITP)*

Immune thrombocytopenia (ITP) is an autoimmune disorder usually associated with anti-platelet antibodies. Platelet depletion reduces the ability of the blood to clot.

ITP was reported in 2% of patients in clinical trials in MS. ITP can be a serious condition leading to morbidity and mortality, and may occur several years after dosing. Prescribers are required to monitor all patients for ITP by obtaining complete blood counts with differential ≤30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the patient's last infusion of LEMTRADA. After this period of time, testing should be performed based on clinical findings suggestive of ITP. Patients should also be monitored for clinical symptoms of ITP. Symptoms of ITP could include (but are not limited to) easy bruising, petechiae, spontaneous mucocutaneous bleeding (epistaxis, hemoptysis), heavier than normal or irregular menstrual bleeding. These clinical signs of ITP may be apparent before serious bleeding develops.

Examples of ITP

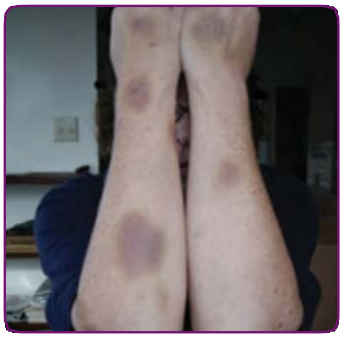
Note: These pictures are only a guide in order to show examples of bruises or petechiae.
The patient may have a less severe type of bruise or petechiae than these pictures and still have ITP.



This is an example of a leg with petechiae.

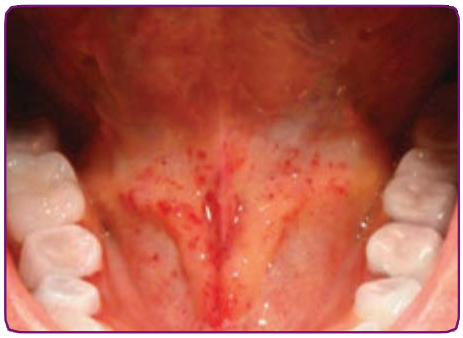
Petechiae are small, scattered, "pin prick" spots under the skin that are red, pink or purple.

Petechiae can occur anywhere on the patient's body, not just the legs.



This is an example of easy or excessive bruising.

This could occur anywhere on the patient's body.



This is an example of purpura under the tongue.

Purpura could occur on any mucous membrane, including anywhere in the mouth (under the tongue, roof of the mouth, inner cheeks, tongue, gums).

• ***Other Autoimmune Cytopenias (including neutropenia, hemolytic anemia, and pancytopenia)***

Autoimmune cytopenias such as neutropenia, hemolytic anemia, and pancytopenia have been infrequently reported in clinical studies in MS. Symptoms of autoimmune hemolytic anemia may include weakness, chest pain, jaundice, dark urine, and tachycardia. Monthly CBC results will also be used to monitor for cytopenias. If a cytopenia is confirmed, appropriate medical intervention should be promptly initiated.

• *Glomerular Nephropathies*

Glomerular nephropathies, including anti-glomerular basement membrane disease (GBM), have been reported after treatment with LEMTRADA in multiple sclerosis patients in clinical trials. Cases of anti-GBM disease have been diagnosed up to 40 months after the last dose of LEMTRADA.

Anti-GBM disease is life-threatening if not treated and therefore demands immediate care. Without prompt treatment, patients can rapidly develop renal failure requiring dialysis and/or kidney transplantation and may lead to death.

Clinical manifestations of nephropathy may include elevation in serum creatinine, hematuria, and/or proteinuria. While not observed in clinical trials, alveolar hemorrhage manifested as hemoptysis may occur with anti-GBM disease. Since patients may be asymptomatic, prescribers are required to monitor patients by obtaining serum creatinine levels and urinalysis with microscopy ≤30 days prior to the first infusion of LEMTRADA and at monthly intervals thereafter until 48 months after the patient's last infusion. After this period of time, testing should be performed based on clinical findings suggestive of nephropathies.

• *Thyroid Disorders*

Autoimmune thyroid disorders occurred in 34% of LEMTRADA-treated patients in clinical studies. Newly diagnosed thyroid disorders occurred throughout the uncontrolled clinical study follow-up period, more than 7 years after the first LEMTRADA dose. Serious thyroid events occurred in 2% of patients. Most thyroid disorders were managed with conventional medical therapy; some patients required surgical intervention. Prescribers are required to monitor all patients for thyroid disorders by obtaining thyroid function tests such as Thyroid Stimulating Hormone (TSH) levels ≤30 days prior to the first infusion of LEMTRADA and then every 3 months thereafter continuing for 48 months following the last infusion. Continue to test thyroid function after 48 months if clinically indicated.

Prescribers should also monitor for signs and symptoms of thyroid disorders, which may include excessive sweating, unexplained weight loss, eye swelling, nervousness and fast heartbeat (hyperthyroidism), or unexplained weight gain, feeling cold, worsening tiredness and newly occurring constipation (hypothyroidism).

- ***Malignancies***

LEMTRADA may increase the risk of thyroid cancer. Patients and Prescribers should monitor for symptoms of thyroid cancer including a new lump or swelling in the neck, pain in the front of the neck, persistent hoarseness or other voice changes, trouble swallowing or breathing, or a constant cough not due to an upper respiratory tract infection.

LEMTRADA may increase the risk of melanoma. Prescribers should perform baseline and yearly skin examinations to monitor for melanoma in patients receiving LEMTRADA.Cases of lymphoproliferative disorders and lymphoma have occurred in LEMTRADA-treated patients with MS.

Strategies to Implement in Your Healthcare Facility to Mitigate Risk of Infusion Reactions:

- Ensure the infusion site is equipped with the necessary equipment and personnel to manage infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).
- Premedicate patients with high dose corticosteroids (1,000 mg of methylprednisolone or equivalent) immediately prior to LEMTRADA infusion and for the first 3 days of each LEMTRADA treatment course. Consider pretreatment with antihistamines and/or antipyretics prior to LEMTRADA administration. Infusion reactions may occur despite pretreatment.
- Observe patients for infusion reactions during and for at least 2 hours after each LEMTRADA infusion.
- Consider longer periods of observation if clinically indicated. Monitor vital signs before and periodically during the infusion.
- Provide appropriate symptomatic treatment as needed if an infusion reaction occurs.
- Consider extending the duration of the infusion if the infusion is not well tolerated.
- Consider immediate discontinuation of the infusion if severe infusion reactions occur.
- Do not administer LEMTRADA outside of the authorized representative's certified healthcare facility.

Proper Storage and Administration

Storage of LEMTRADA

- LEMTRADA is packaged in 12 mg/1.2 mL (10 mg/mL) single-dose vials.
- LEMTRADA vials should be stored at 2° to 8°C (36° to 46°F). Do not freeze or shake. Protect from light.

Prior to Each Treatment Course of LEMTRADA

- Confirm prescriber is certified and patient is enrolled and authorized to receive LEMTRADA.
- Counsel each patient about the risk for infusion reactions.
- Provide the patient with *What You Need to Know about LEMTRADA Treatment and Infusion Reactions: A Patient Guide* prior to dispensing LEMTRADA.
- Administer corticosteroids immediately prior to LEMTRADA administration for the first 3 days of each treatment course.
- Ensure oral prophylaxis for herpes infection is available or has been prescribed to start on the first day of each treatment course Consider pretreating patients with antihistamines and/or antipyretics prior to LEMTRADA administration as needed.
- Monitor vital signs before and periodically during the infusion.

Administration of LEMTRADA

1. Inspect vial for particulate matter/discoloration prior to use.
2. Withdraw 1.2 mL of LEMTRADA from the vial into a syringe using aseptic technique.
3. Inject into 100 mL sterile 0.9% Sodium Chloride USP or 5% Dextrose in Water USP. Gently invert the bag to mix the solution.
4. Cover IV solution bag to protect from light.
5. Administer 12 mg/day over approximately 4 hours.
6. Do **not** administer as IV push or bolus.
7. If infusion is not well tolerated, infusion duration may be extended.
8. Use the LEMTRADA diluted product within 8 hours after dilution LEMTRADA diluted product may be stored at room temperature (15° to 25°C) or refrigerated conditions (2° to 8°C). Protect from light.
9. Monitor patient vital signs before and periodically during the infusion and provide appropriate symptomatic treatment for infusion reactions as needed.
10. Monitor patients for at least 2 hours after each LEMTRADA infusion or longer if clinically indicated.

Following the Conclusion of Each LEMTRADA Treatment Course

- Complete a LEMTRADA REMS Infusion Checklist for each patient at the conclusion of each treatment course or by fax (1-855-557-2478) to the LEMTRADA REMS Program within 5 business days of the last infusion.
- Return unused vials of LEMTRADA to Genzyme within 50 days of receipt of *LEMTRADA REMS Patient Authorization and Baseline Lab Form*.

Adverse Event Reporting

Report suspected adverse events to Genzyme at **1-800-745-4447** (option 2) or to FDA at 1-800-FDA-1088 or **www.FDA.gov/medwatch**.

Genzyme Corporation
500 Kendall Street
Cambridge, MA 02142
Issued: November 2014

US.MS.LEM.14.10.002-v1

LEMTRADA™ alemtuzumab 12mg IV

LEMTRADA REMS Education Program for Prescribers

This education program includes information about:

- The LEMTRADA REMS Program requirements
- Serious risks of autoimmune conditions, infusion reactions and malignancies
- Counseling and management of your patient

LEMTRADA™
alemtuzumab 12mg IV

What is the LEMTRADA REMS Program?

A REMS is a strategy to manage known or potential risks associated with a drug, and is required by the FDA to ensure that the benefits of the drug outweigh its risks. Due to serious risks of autoimmune conditions, infusion reactions and malignancy, LEMTRADA is only available through a restricted program called the LEMTRADA REMS Program.

This brochure has been developed as part of the LEMTRADA REMS Program to help educate prescribers about the risks associated with LEMTRADA and how to help mitigate these risks through periodic monitoring for, and prompt identification of, signs and symptoms of these events.

- **Prescribers** must be enrolled in the LEMTRADA REMS Program to be able to prescribe LEMTRADA.
- **Healthcare facilities and Pharmacies** must be enrolled in the LEMTRADA REMS Program to be able to dispense/ administer LEMTRADA.
- **Patients** must be enrolled and authorized in the LEMTRADA REMS Program in order to receive LEMTRADA.

Steps for Prescriber Certification and Enrollment in the LEMTRADA REMS Program

1. Complete the training program, which includes reviewing the following materials:
   - LEMTRADA Prescribing Information
   - LEMTRADA REMS Program Overview
   - LEMTRADA REMS Education Program for Prescribers
2. Successfully complete the 8-question Knowledge Assessment
3. Enroll in the program by completing a LEMTRADA REMS Prescriber Enrollment Form
4. Submit the completed and signed Forms to the LEMTRADA REMS Program

The LEMTRADA REMS Program Overview, Knowledge Assessment, LEMTRADA Prescribing Information and other REMS materials are available online at **www.LEMTRADAREMS.com** or by contacting the LEMTRADA REMS Program at 1-855-676-6326.

To enroll in the LEMTRADA REMS Program call 1-855-676-6326.

Genzyme will send confirmation of a prescriber's enrollment in the LEMTRADA REMS Program, including the prescriber's assigned LEMTRADA REMS Program identification number.

You will not be able to prescribe LEMTRADA without completing your certification in the LEMTRADA REMS Program.

You should understand that if you fail to comply with the program requirements you may no longer be able to participate in the program.

Overview of Important Safety Information

Indication

LEMTRADA is indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of LEMTRADA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

The Prescribing Information includes a **BOXED WARNING** for LEMTRADA

Please see the Prescribing Information for complete safety information, including BOXED WARNING.

Serious Risks Associated with LEMTRADA

Autoimmune Conditions

LEMTRADA has been associated with risk of autoimmune conditions, including immune thrombocytopenia, other cytopenias (including neutropenia, hemolytic anemia, and pancytopenia), thyroid disorders and glomerular nephropathies, which may occur many years after treatment and may be serious or life-threatening. Early detection can help to improve the outcomes of patients experiencing these events.

Please review the sections that follow to gain a better understanding of the risks of autoimmune conditions.

Immune Thrombocytopenia (ITP)

Immune thrombocytopenia (ITP) occurred in 2% of LEMTRADA-treated patients in clinical studies in MS. Immune thrombocytopenia is an autoimmune disorder usually associated with anti-platelet antibodies. Platelet depletion reduces the ability of the blood to clot. Symptoms of ITP could include (but are not limited to) easy bruising, petechiae, spontaneous mucocutaneous bleeding (epistaxis, hemoptysis), and heavier than normal or irregular menstrual bleeding. These clinical signs of ITP may be apparent before serious bleeding develops.

ITP can be a serious condition leading to morbidity and mortality, and may occur several years after dosing. It is important to monitor all patients for ITP as follows:

- Complete blood counts with differential should be obtained ≤30 days prior to initiation of treatment and at monthly intervals thereafter until 48 months after the patient's last infusion of LEMTRADA. After this period of time, testing should be performed based on clinical findings suggestive of ITP.
- Check the patient for clinical symptoms of ITP.
- Counsel the patient on the importance of complying with monthly monitoring of their blood and the need to continue for 48 months after their last infusion.
- Educate the patient on how to recognize ITP related symptoms, and emphasize the need to remain vigilant for them.
- If ITP is suspected, appropriate medical intervention should be promptly initiated, including immediate referral to a specialist. Severe or widespread bleeding is life-threatening and demands immediate care.

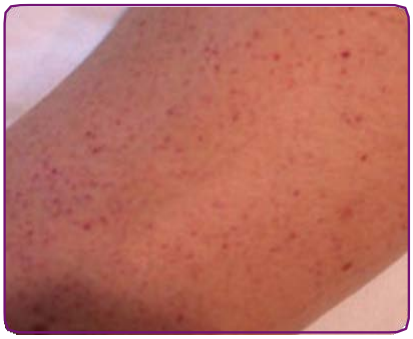
LEMTRADA™ alemtuzumab 12mg IV

Reference ID: 3658409

The potential risk associated with retreatment with LEMTRADA following the occurrence of ITP is unknown.

Examples of ITP

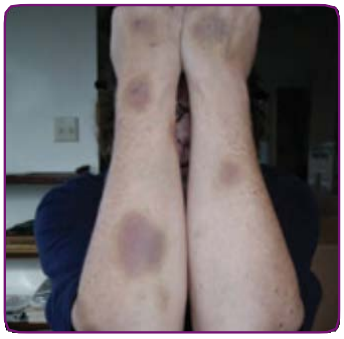
Note: These pictures are only a guide in order to show examples of bruises or petechiae.
The patient may have a less severe type of bruise or petechiae than these pictures and still have ITP.



This is an example of a leg with petechiae.

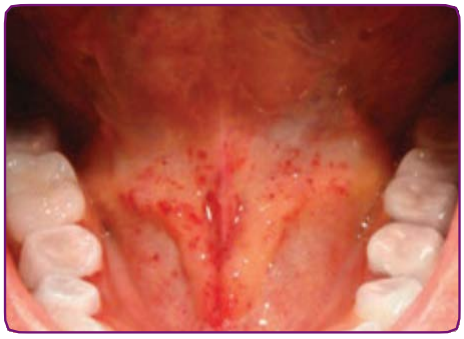
Petechiae are small, scattered, "pinprick" spots under the skin that are red, pink or purple.

Petechiae can occur anywhere on the patient's body, not just the legs.



This is an example of easy or excessive bruising.

This could occur anywhere on the patient's body.



This is an example of purpura under the tongue.

Purpura could occur on any mucous membrane, including anywhere in the mouth (under the tongue, roof of the mouth, inner cheeks, tongue, gums).

> *Other Autoimmune Cytopenias*

Autoimmune cytopenias such as neutropenia, hemolytic anemia, and pancytopenia have been infrequently reported in clinical studies in MS. Symptoms of autoimmune hemolytic anemia may include weakness, chest pain, jaundice, dark urine, and tachycardia. Use the monthly CBC results to monitor for cytopenias. If a cytopenia is confirmed, appropriate medical intervention should be promptly initiated.

> *Glomerular Nephropathies*

Glomerular nephropathies, including anti-glomerular basement membrane (GBM) disease, have been reported after treatment with LEMTRADA in multiple sclerosis patients in clinical trials. Cases of anti-GBM disease have been diagnosed up to 40 months after the last dose of LEMTRADA.

Anti-GBM disease is life-threatening if not treated and therefore demands immediate care. Without prompt treatment, patients can rapidly develop renal failure requiring dialysis and/or kidney transplantation, and this may lead to death.

Clinical manifestations of nephropathy may include elevation in serum creatinine, hematuria, and/or proteinuria.
While not observed in clinical trials, alveolar hemorrhage manifested as hemoptysis may occur with anti-GBM disease. Since patients may be asymptomatic, it is important that the monthly tests are conducted.

- Serum creatinine levels should be obtained ≤30 days prior to the first infusion of LEMTRADA and at monthly intervals thereafter until 48 months after the patient's last infusion. After this period of time, testing should be performed based on clinical findings suggestive of nephropathies.
- Urinalysis with urine cell counts should be obtained ≤30 days prior to the first infusion of LEMTRADA and at monthly intervals thereafter until 48 months after the last infusion. After this period of time, testing should be performed based on clinical findings suggestive of nephropathies. In menstruating females, consider the timing of urinalysis to avoid false positives. The observation of clinically significant changes from baseline in serum creatinine, unexplained hematuria, and/or proteinuria, should prompt further evaluation for nephropathies, including referral to a specialist.
- Early detection and treatment of nephropathies may decrease the risk of poor outcomes.
- Immediate referral to a specialist for further assessment for patients with suspected nephropathy is strongly recommended.

> *Thyroid Disorders*

During clinical trials, autoimmune thyroid disorders including Graves' disease, hyperthyroidism and hypothyroidism were reported. Autoimmune thyroid disorders occurred in 34% of LEMTRADA-treated patients in clinical studies.
Newly diagnosed thyroid disorders occurred throughout the uncontrolled clinical study follow-up period, more than 7 years after the first LEMTRADA dose. Serious thyroid events occurred in 2% of patients. Most thyroid disorders were managed with conventional medical therapy; some patients required surgical intervention.

It is important to monitor all patients for thyroid disorders as follows:

- Thyroid function tests such as Thyroid Stimulating Hormone (TSH) levels should be obtained ≤30 days prior to the first infusion of LEMTRADA and then every 3 months thereafter continuing for 48 months following the last infusion. Continue to test thyroid function after 48 months if clinically indicated.
- Additionally watch out for signs and symptoms of thyroid disorders, which may include excessive sweating, unexplained weight loss, eye swelling, nervousness and fast heartbeat (hyperthyroidism), or unexplained weight gain, feeling cold, worsening tiredness and newly occurring constipation (hypothyroidism).

- Thyroid disease poses special risks in women who become pregnant. Untreated thyroid disease can cause harm to the unborn and newborn baby. Special caution should be taken for pregnant women with Graves' disease, as maternal thyroid stimulating hormone receptor antibodies can be transferred to a developing fetus and can cause transient neonatal Graves' disease. The HCP responsible for managing the patient's pregnancy must be made aware of the increased risk of thyroid disorders due to the patient's LEMTRADA treatment, and the need for these to be appropriately treated.

Strategies to Mitigate the Risk of Autoimmune Conditions

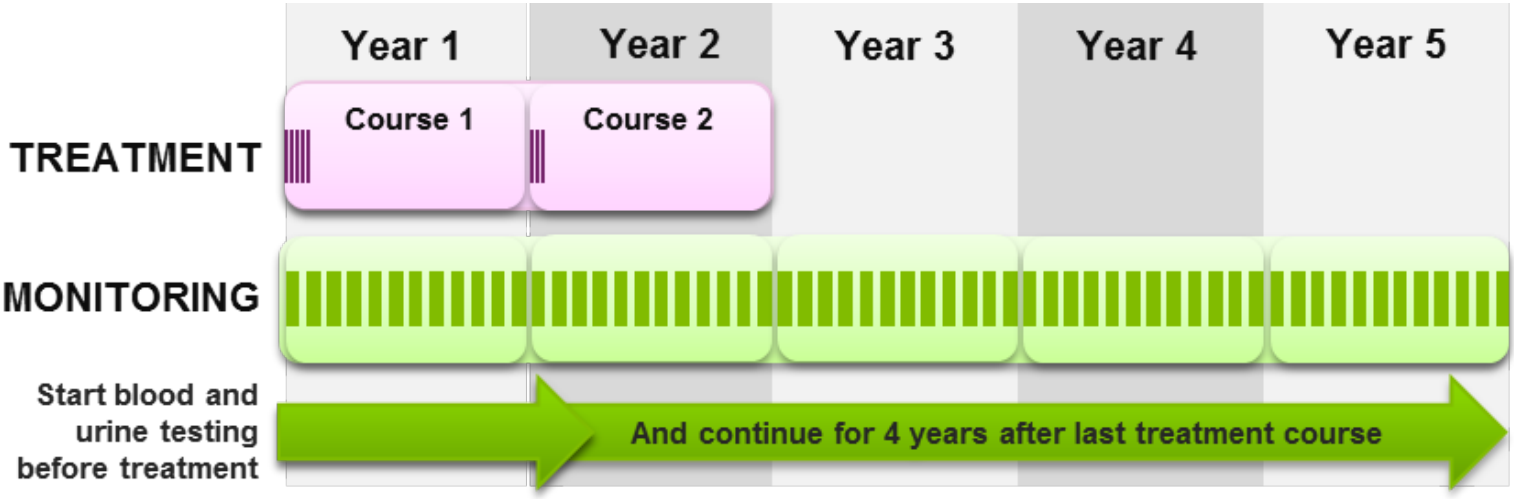
In order to minimize possible risks and side effects of LEMTRADA, prescribers and patients must commit to 48 months of follow-up after the last infusion of LEMTRADA. It is important that patients understand that they should continue with the monitoring, even if they are feeling well.

Creating a partnership between you and your patient, along with careful review of the patient education tool (*What You Need to Know About LEMTRADA Treatment: A Patient's Guide*) with your patient, will help patients to:

- Comply with periodic tests
- Identify and report symptoms early
- Receive prompt and appropriate treatment if needed

To enhance your understanding of the duration of the effects of treatment and the length of required follow-up, please refer to the diagrams below titled ***Overview of LEMTRADA Treatment*** and ***Overview of LEMTRADA Monitoring***.

Overview of LEMTRADA Treatment



Overview of LEMTRADA Monitoring

Condition	Activity	Timing	
Immune Thrombocytopenia(ITP)	Complete blood count With differential	Prior to initiating LEMTRADA treatment	Monthly until 48 months after last infusion
Glomerular Nephropathies, including anti-GBM disease	Serum creatinine	Prior to initiating LEMTRADA treatment	Monthly until 48 months after last infusion
Glomerular Nephropathies, including anti-GBM disease	Urinalysis with microscopy	Prior to initiating LEMTRADA treatment	Monthly until 48 months after last infusion
Thyroid Disorders	Thyroid function tests (such as TSH)	Prior to initiating LEMTRADA treatment	Every 3 months until 48 months after last infusion

Infusion Reactions

Most patients treated with LEMTRADA in controlled clinical trials in MS experienced infusion reactions during or after LEMTRADA administration. . In some patients, infusion reactions were reported more than 24 hours after LEMTRADA infusion. Serious reactions occurred in 3% of patients, including cases of anaphylaxis in 2 patients (including anaphylactic shock), angioedema, bronchospasm, hypotension, chest pain, bradycardia, tachycardia (including atrial fibrillation), transient neurologic symptoms, hypertension, headache, pyrexia and rash. Other infusion reactions included nausea, urticaria, pruritus, insomnia, chills, flushing, fatigue, dyspnea, pulmonary infiltrates, dysgeusia, dyspepsia, dizziness and pain. In clinical studies, 0.6% of patients with infusion reactions received epinephrine or atropine.

Premedicate with high dose corticosteroids (1,000 mg of methylprednisolone or equivalent) immediately prior to LEMTRADA infusion and for the first 3 days of each treatment course. Consider pretreatment with antihistamines and/or antipyretics prior to LEMTRADA administration. Infusion reactions may occur in patients despite pretreatment.

LEMTRADA can only be administered in certified healthcare settings that have on-site access to equipment and personnel trained to manage infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).

Patients must be observed for infusion reactions during and for at least 2 hours after each LEMTRADA infusion. Consider longer periods of observation if clinically indicated. Vital signs should be monitored before the infusion and periodically during the infusion. If an infusion reaction occurs, appropriate symptomatic treatment should be provided as needed. The duration of the infusion may be extended if clinically indicated. If severe infusion reactions occur, immediate discontinuation of the infusion should be considered.

LEMTRADA™ alemtuzumab 12mg IV

Malignancies

LEMTRADA is an immunomodulatory therapy and caution should be exercised in initiating LEMTRADA in patients with pre-existing or ongoing malignancies.

> *Thyroid Cancer*

LEMTRADA may increase the risk of thyroid cancer. In controlled clinical studies 0.3% LEMTRADA-treated patients developed thyroid cancer, compared to none in the interferon beta-1a-treated group. However, screening for thyroid cancer was performed more frequently in the LEMTRADA-treated group, because of the higher incidence of autoimmune thyroid disorders in those patients. Two additional cases of thyroid cancer in LEMTRADA-treated patients occurred in uncontrolled studies.

> *Melanoma*

LEMTRADA may increase the risk of melanoma. In uncontrolled studies, 0.3% LEMTRADA-treated patients developed melanoma or melanoma in situ. One of those patients had evidence of locally advanced disease.

> *Lymphoproliferative Disorders and Lymphoma*

Cases of lymphoproliferative disorders and lymphoma have occurred in LEMTRADA-treated patients with MS, including a MALT lymphoma, Castleman's Disease, and a fatality following treatment of non-Epstein Barr Virus-associated Burkitt's lymphoma. There are postmarketing reports of Epstein Barr Virus associated lymphoproliferative disorders in non-MS patients.

> *Monitoring for Malignancies*

Patients and healthcare providers should monitor for symptoms of thyroid cancer including a new lump or swelling in the neck, pain in the front of the neck, persistent hoarseness or other voice changes, trouble swallowing or breathing, or a constant cough not due to an upper respiratory tract infection.

Perform baseline and yearly skin examinations to monitor for melanoma in patients receiving LEMTRADA.

Patient Enrollment, Counseling and Management

To enroll your patient in the LEMTRADA REMS Program, you must:

- Complete the *LEMTRADA REMS Patient Enrollment Form* for each patient and provide a completed copy to the patient. The completed form should be submitted to the LEMTRADA REMS Program and a copy stored in the patient's records.
- Enrollment forms can be obtained online (www.LEMTRADAREMS.com) or by phone (1-855-676-6326).
- Completed forms should be faxed to 1-855-557-2478.
- Genzyme will provide confirmation of patient enrollment.

As part of patient management and counseling, you must:

- Inform your patient about the risks associated with LEMTRADA, including the risks of autoimmune conditions, infusion reactions, and malignancies, and the need for baseline and periodic monitoring. A patient directed educational guide has been developed for you to use in counselling your patients on the risks associated with LEMTRADA (*What You Need to Know About LEMTRADA Treatment: A Patient Guide*). You should review this guide with your patient on an ongoing basis. You must provide each patient with a copy of this guide and a *LEMTRADA Patient Safety Information Card*.
- Perform the baseline and periodic monitoring described above and in the Prescribing Information for LEMTRADA.
- Complete the *LEMTRADA REMS Patient Status Form* 6 months after the patient's first infusion with LEMTRADA, and every 6 months thereafter, until 48 months after the completion of the patient's last infusion of LEMTRADA and submit the completed form to the LEMTRADA REMS Program.
- Notify Genzyme if an enrolled patient who has received LEMTRADA within the last 48 months is no longer under your care.

Ordering LEMTRADA

To order LEMTRADA, you must submit a *LEMTRADA REMS Prescription Ordering Form* for each LEMTRADA prescription to the LEMTRADA REMS Program. The ordering form can be obtained online (www.LEMTRADAREMS.com) or by phone (1-855-676-6326). Completed forms should be faxed to 1-855-557-2478.

Administering LEMTRADA

As part of the LEMTRADA REMS Program, a healthcare facility must be enrolled in the LEMTRADA REMS Program to be able to dispense/administer LEMTRADA. It is important that you select a healthcare facility that is enrolled and active in the LEMTRADA REMS Program for your patient's infusion. A database of certified healthcare facilities is available by phone at 1-855-676-6326.

Prior to your patient's infusion, you must submit *a LEMTRADA REMS Patient Authorization and Baseline Lab Form* to the LEMTRADA REMS Program indicating completion of each patient's baseline labs within 30 days of the infusion date.

Prior to Each Treatment Course of LEMTRADA

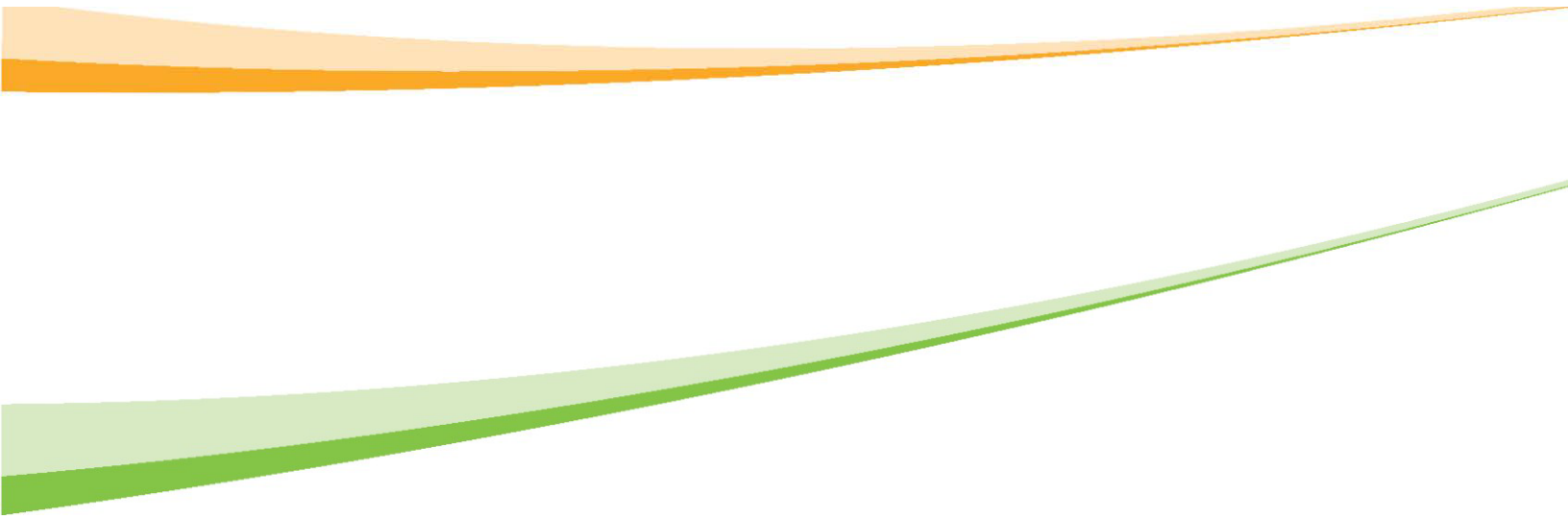
- Administer corticosteroids (1,000 mg methylprednisolone or equivalent) immediately prior to LEMTRADA administration for the first 3 days of any treatment course
- Administer anti-viral prophylaxis for herpetic viral infection starting on the first day of each treatment course and continuing for a minimum of 2 months following treatment with LEMTRADA or until the CD4+ lymphocyte count is ≥200 cells per microliter, whichever occurs later
- Consider pretreating patients with antihistamines and/or antipyretics prior to LEMTRADA administration as needed

Adverse Event Reporting

Report suspected adverse events to Genzyme at **1-800-745-4447** (option 2) or to FDA at 1-800-FDA-1088 or **www.FDA.gov/medwatch**.

Genzyme Corporation
500 Kendall Street
Cambridge, MA 02142
Issued: November 2014

LEMTRADA™ alemtuzumab 12mg IV



LEMTRADA™
alemtuzumab 12mg IV

For Healthcare Providers

LEMTRADA REMS Knowledge Assessment

To become a certified prescriber in the LEMTRADA REMS Program you will need to answer ALL 8 questions correctly.

> Complete the Knowledge Assessment, populate and sign the one-time LEMTRADA REMS Prescriber Enrollment Form. Fax your responses to all 8 Knowledge Assessment questions and LEMTRADA REMS Prescriber Enrollment Form to 1-855-557-2478.

> You will receive correspondence from the LEMTRADA REMS Program via the preferred communication method (email or fax) selected on your enrollment form within two business days. Correspondence may include:

- How to retake the Knowledge Assessment, if necessary
- A confirmation of your enrollment and certification in the LEMTRADA REMS Program (which requires no further action)

LEMTRADA™
alemtuzumab 12mg IV

QUESTIONS 1-8

QUESTION 1 (check one)

Which of the following laboratory tests are required prior to initiating LEMTRADA treatment and within 30 days of the first infusion?

- ☐ A. Complete Blood Count (CBC) with differential
- ☐ B. Serum creatinine and urinalysis with urine cell counts
- ☐ C. Thyroid function test
- ☐ D. All of the above

QUESTION 2 (check one)

My patient must have monthly blood and urine tests for:

- ☐ A. 12 months after their last infusion
- ☐ B. 24 months after their last infusion
- ☐ C. 36 months after their last infusion
- ☐ D. 48 months after their last infusion

QUESTION 3

I should assess my patient's compliance with required lab testing on an ongoing basis and document their compliance on the LEMTRADA REMS Patient Status Form every 6 months.

- ☐ True
- ☐ False

QUESTION 4 (check one)

Which of the following symptoms could be associated with Immune Thrombocytopenia (ITP)?

- ☐ A. Headache, rash, pyrexia, nausea
- ☐ B. Easy bruising, petechiae, purpura, spontaneous mucocutaneous bleeding
- ☐ C. Weight gain, fatigue, constipation
- ☐ D. Pyrexia, chills, swollen glands

QUESTION 5 (check one)

Which of the following could be associated with Glomerular Nephropathy?

- ☐ A. Elevation in serum creatinine, hematuria or proteinuria
- ☐ B. Easy bruising, petechiae, purpura, spontaneous mucocutaneous bleeding (e.g., epistaxis, hemoptysis), and heavier than normal or irregular menstrual bleeding
- ☐ C. Weight gain, fatigue, constipation
- ☐ D. Weight loss, tachycardia, nervousness

QUESTION 6 (check one)

Prior to enrolling a patient in the LEMTRADA REMS Program, you should:

- ☐ A. Provide "What You Need to Know About LEMTRADA Treatment: A Patient Guide" to the patient
- ☐ B. Counsel the patient on the serious risks associated with LEMTRADA and how to mitigate these risks through periodic monitoring
- ☐ C. Provide a LEMTRADA Patient Safety Information Card to the patient
- ☐ D. All of the above

QUESTION 7

The healthcare facility that will administer LEMTRADA infusions to my patient is not required to be REMS certified and enrolled.

- ☐ True
- ☐ False

QUESTION 8

LEMTRADA treatment should be administered in a setting that has the necessary equipment and personnel to manage serious infusion reactions (including anaphylaxis and cardiac and respiratory emergencies).

- ☐ True
- ☐ False

Please provide your Prescriber name and NPI so we can associate your progress with your stakeholder record. You can provide this information below.

Prescriber Name:_____

Prescriber NPI: _____

LEMTRADA™
alemtuzumab 12mg IV

<Date>

«Patient_First_Name» «Patient_Last_Name»
«Patient_Address_2»
«Patient_Address_1»
«Patient_City», «Patient_State» «Patient_Zip»

Dear «Patient_First_Name» «Patient_Last_Name»:

When enrolling in the LEMTRADA™ REMS Program, you and your doctor agreed that you will participate in monthly laboratory monitoring for 4 years after your last infusion to monitor for possible side effects.

The lab tests, which are required every 30 days, are important to identify side effects like autoimmune conditions. Please make sure to continue to schedule and go to your monthly lab appointments.

It is also important that you look for symptoms of these side effects by doing your own symptom self-checks, as described in the Patient Guide (*What You Need to Know About LEMTRADA Treatment: A Patient Guide*) that your doctor gave you before you started your LEMTRADA treatment.

As part of the program, you are receiving these monthly reminders for your lab tests. For your convenience, the program offers options on how you can receive your monthly reminders:

- By mail
- By phone
- By email

If you wish to change the way you receive these reminders, please call the LEMTRADA REMS Program at 1-855-676-6326.

If you have questions about LEMTRADA or your monthly lab monitoring, please call the LEMTRADA REMS Program at 1-855-676-6326, Monday through Friday, 8:30 AM to 8:00 PM EST. In addition, please contact the LEMTRADA REMS Program if your contact information has changed.

Sincerely,

LEMTRADA REMS Program

genzyme
A SANOFI COMPANY | www.genzyme.com

LEMTRADA™
alemtuzumab 12mg IV

[Date]

[Treating Provider First Name] [Treating Provider Last Name], [Treating Provider Title]
[Treating Correspondence Primary Contact First Name] [Treating Correspondence Primary Contact Last Name]
[Treating Site Name]
[Treating Site Address 2]
[Treating Site Address 1]
[Treating Site City, State Zip]

RE: Prescriber LEMTRADA™ (alemtuzumab) REMS Program Responsibilities Reminder

Dear Dr. [Provider Last Name],

This letter is to remind you of your responsibilities as a prescriber enrolled in the LEMTRADA REMS Program. Please remember that you must:

1. **Keep Track of needed Lab Monitoring**: Prescribers are required to keep track of the laboratory monitoring status of all patients who have been infused with LEMTRADA from first infusion until 48 months after the last infusion.

2. **Complete LEMTRADA REMS Status Forms**: For every patient who is infused with LEMTRADA, prescribers are required to complete a LEMTRADA REMS Patient Status Form six months after the first infusion, and then every subsequent six months until 48 months after the patient's last infusion.

If you have any questions about requirements, please call the LEMTRADA REMS Program at 1-855-676-6326, Monday through Friday, 8:30AM to 8:00PM Eastern Standard Time.

Sincerely,

LEMTRADA REMS Program

genzyme A SANOFI COMPANY | www.genzyme.com

LEMTRADA™ alemtuzumab 12mg IV

LEMTRADA
alemtuzumab 12mg IV

LEMTRADA Prescription Ordering Form

Please fax this completed form to 1-855-557-2478

*Indicates a mandatory field.

I: PATIENT INFORMATION (PLEASE PRINT)

Name (First, Last)*		
Date of Birth (MM/DD/YYYY)*	Gender* ☐Male ☐Female	
Street Address 1*		
Street Address 2*		
City*	State*	ZIP Code*
Phone Number*		

THIS SECTION SHOULD BE FILLED OUT BY YOUR HEALTHCARE PROVIDER

II: INSURANCE INFORMATION

Patient does not have insurance. ☐

Primary Insurance Company*	Phone Number*	Name of Insured*	Policy Number*	Group/Policy Number*
Secondary Insurance Company	Phone Number	Name of Insured	Policy Number	Group/Policy Number

III: PRESCRIBER INFORMATION

Prescriber Name (First, Last)*	NPI Number*	Name of Institution or Facility*		Tax ID*	
Office Contact*		Street Address*	City*	State*	ZIP Code*
Email Address		Phone Number*	FaxNumber*		

IV: PRESCRIPTION INFORMATION

Lemtrada (alemtuzumab) 12mg IV

Check one* ☐Initial course (1 vial [12 mg/day]) X 5 consecutive days Number of vials:_____

☐Subsequent course (1 vial [12mg/day]) X 3 consecutive days Number of vials:_____ Primary diagnosis: ICD-9 CM340

V: INFUSION CENTER INFORMATION[§]

Infusion Center Where Patient Is Referred*	Phone Number*	
Street Address*		
City*	State*	ZIP Code*

[†]LEMTRADA is a trademark of Genzyme Corporation and GENZYME is a registered trademark of Genzyme Corporation.

[§]Note: LEMTRADA can only be infused at authorized infusion sites. Genzyme Corporation will contact you if the infusion center you have indicated is not authorized to infuse LEMTRADA.

***Note to Prescribers**: This form does not authorize the certified pharmacy or infusion center to dispense LEMTRADA. The LEMTRADA REMS Patient Authorization and Baseline Lab form must be submitted in order to authorize LEMTRADA to be dispensed.

By signing below, I authorize the LEMTRADA REMS Program and its agents and representatives to forward this prescription on my behalf to a certified pharmacy or infusion center to dispense LEMTRADA to the patient named above.

X

Licensed Prescriber Signature* (Signature required; no stamps accepted) Print Name* Date*

Reference ID: 3658409

For Patients

LEMTRADA™ (alemtuzumab) What You Need to Know About LEMTRADA Treatment: A Patient Guide

Patients: Your doctor or nurse will go over this Patient Guide with you. It is important to ask any questions you might have prior to each time LEMTRADA is given to you. Keep this guide for important safety information about the serious risks and reactions of LEMTRADA.

Healthcare Providers: Review this Patient Guide with your patient prior to each treatment course and provide your patient a copy to take home.

Reference ID: 3658409

What is LEMTRADA?

LEMTRADA is a prescription medicine approved to treat adult patients with relapsing forms of multiple sclerosis and because of its serious risks it is generally reserved for patients that have not been helped enough by 2 or more MS treatments. You and your healthcare provider have determined that LEMTRADA is an appropriate treatment for you.

LEMTRADA is only available at your doctor's office, clinic or hospital. It is not a medicine you will give yourself at home because of the serious risks of LEMTRADA.

What is the Most Serious Risk Information about LEMTRADA Treatment?

LEMTRADA may cause serious side effects, including infusion reactions, autoimmune conditions and malignancy.

- Most patients treated with LEMTRADA will experience side-effects at the time of the infusion or within 24 hours after the infusion (**infusion reactions**). Common infusion reactions include nausea, hives, itching, difficulty sleeping, chills, flushing, fatigue, shortness of breath, congestion of the lungs, upset stomach, dizziness and pain.
- Patients receiving LEMTRADA are at risk of **autoimmune conditions**. Your body's immune system contains particular cells that help fight infections. Autoimmune side effects are illnesses that occur when these cells of the immune system fight against your own body.
- Receiving LEMTRADA may increase your chance of getting some kinds of cancers (malignancies), including thyroid cancer, skin cancer (melanoma), and blood cancers called lymphoproliferative disorders and lymphoma. Call your healthcare provider if you have the following symptoms that may be a sign of thyroid cancer:
  - new lump
  - swelling in your neck
  - pain in the front of your neck
  - hoarseness or other voice changes that do not go away
  - trouble swallowing or breathing
  - cough that is not caused by a cold

You should have your skin checked before you start receiving LEMTRADA and each year while you are receiving treatment to monitor symptoms of skin cancer.

What are the Signs and Symptoms of Infusion Reactions, and Autoimmune Conditions After LEMTRADA Treatment, and What Should I Do?

Infusion reactions

Most patients treated with LEMTRADA will experience side-effects at the time of the infusion, some of which may be serious or life threatening. Serious infusion reactions may happen while you receive, or up to 24 hours or longer after you receive LEMTRADA.

Tell your healthcare provider right away if you have any of the following symptoms of a serious infusion reaction during the infusion or after you have left the healthcare facility:

- swelling in your mouth or throat
- trouble breathing
- weakness
- fast, slow, or irregular heart beat
- chest pain
- rash

In order to try to reduce these effects, your doctor will give you medication (corticosteroids) prior to the first 3 infusions of a treatment course. You may also be given other treatments before or after the infusion to try to reduce your chances of these reactions or to treat them after they happen. In addition, you will be observed during the infusion and for at least 2 hours after the infusion has been completed or longer if your healthcare provider decides you need to stay longer. In case of serious reactions, it is possible that the infusion may be stopped.

Delayed side effects

As mentioned previously, patients receiving LEMTRADA are at risk of certain autoimmune conditions. The autoimmune conditions include:

- Immune thrombocytopenia (ITP, or low platelets)
- Other blood disorders (including neutropenia, hemolytic anemia, and pancytopenia)
- Certain types of kidney diseases
- Thyroid disorders

All of these conditions can be treated when identified early, but delaying treatment increases the risk of complications. This is why it is so important to recognize and immediately report any signs or symptoms of these conditions to your doctor.

In the following pages, you will learn more about each of these side effects, including the signs and symptoms that you may experience and what to do if they hap pen.

Immune Thrombocytopenia (ITP, or low platelets)

ITP is a condition which results in a decrease in the number of platelets in the blood. ITP has been observed in approximately 2% of patients treated with LEMTRADA in MS clinical trials. Platelets are necessary for normal blood clotting. ITP can cause severe bleeding. If detected early, ITP is usually treatable, but if left untreated it may lead to serious health problems and possibly death.

A blood test will help your doctor watch for changes in your platelet count in order to catch this side effect early. Therefore, your doctor will have your blood tested before starting LEMTRADA and on a monthly basis after your first infusion. The monthly testing must continue for 4 years after your last infusion or longer if you have signs or symptoms of ITP.

Importantly, ITP may also be detected by certain signs or symptoms that you need to be aware of.

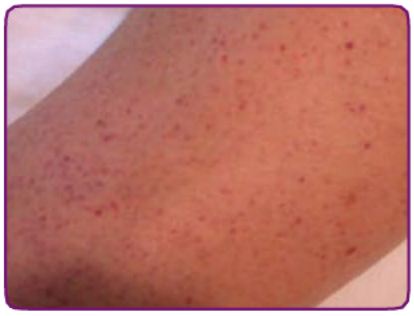
What are the signs and symptoms of ITP?

- Small scattered spots on your skin that are red, pink or purple
- Easy bruising
- Bleeding from a cut that is harder to stop
- Heavier, longer or more frequent menstrual periods than normal. Bleeding between your menstrual periods could also be a sign of ITP
- Bleeding from your gums or nose that is new or takes longer than usual to stop

Call your doctor immediately if you have any of these signs or symptoms. If you cannot reach your doctor, seek immediate medical attention.

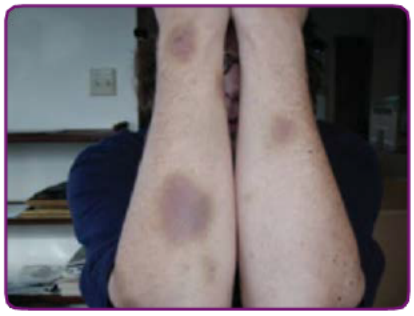
LEMTRADA™ alemtuzumab 12mg IV

These pictures show examples of spots and bruises caused by ITP.



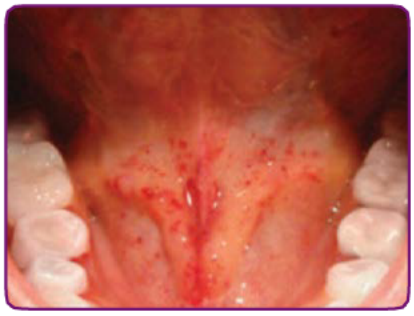
This is an example of a leg with scattered spots under the skin that are red, pink or purple. They might look like pin pricks.

It is important to note that the spots could occur anywhere on your body, not just on your leg.



This is an example of arms with easy or excessive bruising.

It is important to note bruises could occur anywhere on your body, not just on your arms.



This is an example of spots due to bleeding under the tongue.

It is important to note that this could occur anywhere in your mouth—under the tongue, on the roof of your mouth, on your inner cheeks, on your tongue, or on your gums.

Note: These pictures are only a guide in order to show examples of bruises or rashes

What if I develop ITP?

It is best to identify and treat ITP as early as possible. That is why it is so important that you continue to have your monthly blood test and check for symptoms, which could detect a problem before you have symptoms. It is also important that you, your family members, and/or caregivers are watching for any of the signs or symptoms described in this guide. Delaying treatment of ITP raises the chance of more serious problems.

If detected early, ITP is usually treatable. If you develop ITP, you and your doctor will decide which treatment is best for you.

If you notice any of the signs or symptoms as described above, call your healthcare provider right away to report the symptoms. If you cannot reach your healthcare provider, seek immediate medical attention.

Other blood disorders (including neutropenia, hemolytic anemia, and pancytopenia)

LEMTRADA may case a decrease in some type of blood cells. Symptoms may include weakness, dark urine, chest pain, yellowing of the skin or whites of your eyes (jaundice), or fast heartbeat. Your healthcare provider will do blood tests to check for low blood counts.

Kidney disorders (such as anti-glomerular basement membrane disease)

LEMTRADA may cause a condition known as anti-glomerular basement membrane disease, or anti-GBM disease. Kidney disorders, including anti-GBM disease, have been observed in 0.3% (3 per 1,000) patients treated with LEMTRADA in MS clinical trials. Anti-GBM disease is an autoimmune side effect that can result in severe damage to the kidneys. Anti-GBM disease can also damage the lungs, although this was not seen in clinical trials with LEMTRADA. If untreated it can cause kidney failure requiring chronic dialysis or transplant, and may lead to death. Most of the time, doctors can treat kidney problems. It is best to begin treatment as early as possible.

A blood test and a urine test will help your doctor watch for signs of kidney disease to help catch this potential side effect early. Your doctor will have your blood and urine tested in the month before you start treatment with LEMTRADA and on a monthly basis after your initial infusion. Your doctor will test your urine monthly, so if you are a woman, it is important to avoid urine testing during your menstrual period as this may give a false result. This testing will continue for 4 years after your last infusion or longer if you have signs or symptoms of a kidney disorder.

Importantly, anti-GBM disease can also be detected by certain signs and symptoms that you need to be aware of.

What are the signs and symptoms of kidney problems or anti-GBM disease?

- Blood in the urine (red or tea-colored urine)
- Swelling in your legs or feet
- Coughing up blood

What if I develop kidney problems?

It is best to begin treatment as early as possible. It is important that you are familiar with the signs and symptoms of kidney problems and anti-GBM disease, and complete your regular laboratory tests (blood tests and urine tests). Kidney problems will almost always need treatment.

If you notice any of the signs or symptoms as described above, call your doctor right away to report the symptoms. If you cannot reach your doctor, seek immediate medical attention.

LEMTRADA™
alemtuzumab 12 mg IV

Thyroid disorders

The thyroid is a gland found in the lower part of the neck. This gland produces hormones that are important throughout your body. In some people, the immune system may mistakenly attack the cells of the thyroid gland (autoimmune thyroid condition) which affect its ability to make and control the level of hormones.

LEMTRADA may cause development of thyroid disorders including:

- Overactive thyroid gland, or hyperthyroidism, when the thyroid produces too much hormone
- Underactive thyroid gland, or hypothyroidism, when the thyroid does not produce enough hormone

An estimated 34% of patients experienced autoimmune thyroid disorders following treatment with LEMTRADA in MS clinical trials.

Your blood will be checked in the month before you start treatment with LEMTRADA and every 3 months after your initial infusion until 4 years after your last LEMTRADA infusion or longer if you show signs or symptoms of a thyroid disorder. This blood test will help your doctor detect thyroid disorders early.

What are the signs and symptoms of a thyroid disorder?

Overactive thyroid, or hyperthyroidism	Underactive thyroid, or hypothyroidism
> Excessive sweating	> Unexplained weight gain
> Unexplained weight loss	> Feeling cold
> Eye swelling	> Worsening tiredness
> Nervousness	> Newly occurring constipation
> Fast heartbeat	

What if I develop a thyroid disorder?

Tell your doctor if you experience these symptoms. Most of the time, thyroid disorders are manageable with treatment. Depending on the type of thyroid disorder, your doctor will decide which treatment is best for you. It will be important to follow your doctor's recommendations to be sure to benefit the most from your treatment. In some cases, you may have to take medication for the rest of your life for your thyroid disorder. In some situations, your thyroid may need to be removed.

If you develop a thyroid disorder, it is very important that you are properly treated for it, especially if you become pregnant after using LEMTRADA. Having an untreated thyroid disorder could harm your unborn baby, or harm your baby after birth.

IMPORTANT!

Since all of these autoimmune conditions could occur long after you received a course of treatment with LEMTRADA, it is very important that you continue to have your monthly blood and urine tests (even if you are feeling well).

⚠ **You must continue to watch for signs and symptoms**

⚠ **Do this for 4 years after your last LEMTRADA infusion**

⚠ **Early detection and prompt treatment may give you the best opportunity for improvement**

Carry your LEMTRADA Patient Safety Information Card with you at all times and show it to any healthcare professionals who are providing you treatment (including for non-MS conditions) or in the event of a medical emergency.

These are **NOT** all the possible side effects of LEMTRADA. Refer to the LEMTRADA Medication Guide that you were given or talk to your doctor or nurse for medical advice about other side effects.

LEMTRADA™
alemtuzumab 12mg IV

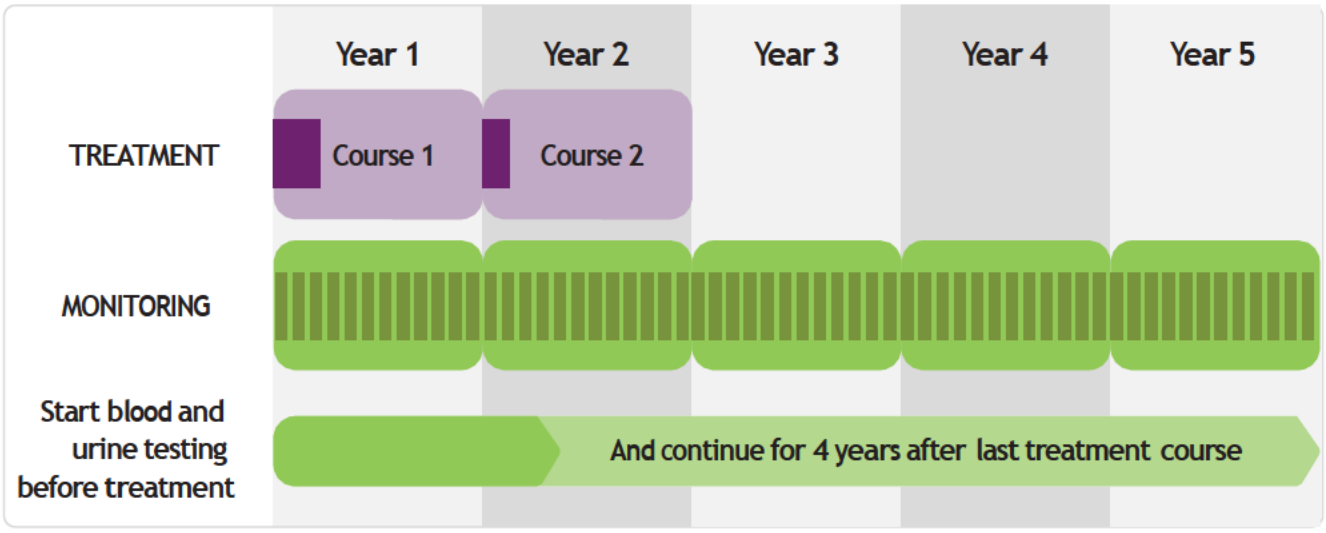
How Can I Detect the Delayed Side Effects from LEMTRADA?

To check for the development of autoimmune conditions (previously described), you will have to be monitored monthly by having your blood and urine tested. Your doctor will order blood and urine tests in the month before you start LEMTRADA treatment and these tests will continue each month for 4 years after your last LEMTRADA infusion. Monitoring may need to continue for longer if you have signs or symptoms of autoimmune conditions. Your doctor will check the results of these tests to see if you have developed any side effects.

It is very important that you continue to have these tests for 4 years after your last LEMTRADA infusion, even if you are feeling well (no symptoms or side effects) . Side effects may occur many months to years after your LEMTRADA infusion and may be (in rare cases) life-threatening, so it is very important that you continue to be checked and that you watch out for symptoms. This will help allow a problem to be detected and treatment to begin right away.

This means that you commit to the monthly blood and urine laboratory tests, continuing for 4 years after your last infusion with LEMTRADA . You and your doctor will work together as a team to make sure you get these tests done, and to plan them around your normal activities. If you are a woman, it is also important to avoid urine testing during your menstrual period, as this may give a false result.

To help you better understand the duration of the effects of LEMTRADA treatment and the length of required follow-up, please refer to the diagram below.



The following table shows you which laboratory tests are done, when, and for how long.

Test	When?	For how long?
Blood tests	Before treatment starts and every month after treatment	For 4 years after your last LEMTRADA infusion
Urine tests	Before treatment starts and every month after treatment	For 4 years after your last LEMTRADA infusion

How is LEMTRADA Given?

You will receive LEMTRADA through an intravenous line in your vein (infusion). LEMTRADA is given in two treatment courses. Generally, you will receive LEMTRADA for 5 days for the first treatment course and then for 3 days approximately 1 year later (second treatment course).

The infusion takes place in a healthcare facility or infusion center. It takes about 4 hours to receive a full dose each day, but can take longer if you have side effects (infusion reactions), in which case the infusion may need to be slowed down or stopped. In order to try to reduce some of these reactions, your doctor will give you medication (corticosteroids) prior to the first 3 infusions of a treatment course. You may also be given other treatments before, during, or after the infusion to try to avoid these reactions or to treat them once they happen. In addition, you will be observed during the infusion and for at least 2 hours after the infusion has been completed or longer if your healthcare provider decides you need to stay longer. In case of serious reactions, it is possible that the infusion may be stopped.

Where Can I Get More Information on LEMTRADA?

There is a LEMTRADA Medication Guide that your doctor or nurse will give you at the beginning of your treatment course. You can also find additional information at www.LEMTRADAREMS.com or call the LEMTRADA REMS Program at 1-855-676-6326.

How Can I Reach My Doctors?

To make it easier to contact your doctor(s) or your healthcare team, please fill in their telephone numbers and addresses in the chart below.

Doctor/Healthcare Team	Telephone Number	Address

Genzyme Corporation
500 Kendall Street
Cambridge, MA 02142
Issued: November 2014

LEMTRADA™
alemtuzumab 12mg IV

For Prescribers to Complete

LEMTRADA™ alemtuzumab 12mg IV

LEMTRADA REMS PATIENT AUTHORIZATION AND BASELINE LAB FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478.

This form must be completed within 30 days prior to the first infusion date of each LEMTRADA patient's treatment course.

*Indicates a mandatory field.

PRESCRIBER INFORMATION (PLEASE PRINT)

Name (first, last)* | Office Phone Number*

Address*

City* | State* | ZIP Code*

Prescriber LEMTRADA REMS Program Identification Number*

PATIENT INFORMATION (PLEASE PRINT)

Name (first, last)*

Patient LEMTRADA REMS Program Identification Number*

Date of Birth (MM/DD/YYYY)*

AUTHORIZATION AND BASELINE LABS

Do you authorize LEMTRADA treatment for the above-referenced patient?* ☐ Yes ☐ No

Do you attest that required baseline laboratory testing has been completed prior to LEMTRADA treatment and within 30 days of the patient's first infusion?* ☐ Yes ☐ No

PRESCRIPTION INFORMATION

Check one* ☐ Initial course (1 vial [12 mg/day]) X 5 consecutive days — Number of vials: ____

☐ Subsequent course (1 vial [12mg/day]) X 3 consecutive days — Number of vials: ____

PRESCRIBER'S SIGNATURE

Prescriber Signature* | Date*

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

genzyme A SANOFI COMPANY

For Pharmacy

LEMTRADA™ alemtuzumab 12mg IV

LEMTRADA REMS PHARMACY ENROLLMENT FORM

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

LEMTRADA™ (alemtuzumab) is only available through the LEMTRADA REMS Program, a restricted distribution program. Only prescribers, pharmacies, healthcare facilities, and patients enrolled in the program are able to prescribe, dispense, administer, and receive LEMTRADA. An authorized representative of the Pharmacy must enroll the pharmacy in the LEMTRADA REMS Program.

☐ New Enrollment
☐ Re-enrollment (every 2 years)

*Indicates a mandatory field.

PHARMACY INFORMATION (Please Print)

Name of Pharmacy*		NPI Number*	
Pharmacy Address*			
City*		State*	ZIP Code*
Name of Authorized Pharmacy Representative*		Title*	
Phone Number*	Fax Number*	Email Address	

PHARMACY AGREEMENT

I am the Authorized Representative designated by my Pharmacy to coordinate the activities of the LEMTRADA REMS Program. By signing this form, I agree to comply with the following program requirements:

- I understand that my Pharmacy must be certified with the LEMTRADA REMS Program to dispense LEMTRADA.
- I will oversee implementation and compliance with the LEMTRADA REMS Program requirements.
- I have reviewed the LEMTRADA REMS Program Overview.
- I will ensure that all relevant staff involved in the dispensing of LEMTRADA are educated and trained using the LEMTRADA REMS Program Overview.
- I will put processes and procedures in place, and follow such processes and procedures, to ensure the following verifications are met prior to dispensing LEMTRADA:
  - The LEMTRADA REMS Prescription Ordering Form is received for each prescription.
  - The prescriber is certified, the infusion site is certified, and the patient is enrolled and authorized to receive LEMTRADA by contacting the LEMTRADA REMS Program prior to dispensing LEMTRADA.
  - Ensuring LEMTRADA is only dispensed to a certified infusion center.
- This Pharmacy will establish procedures and protocols that are subject to audit, to help ensure compliance with the requirements of the LEMTRADA REMS Program.
- I understand that my Pharmacy must renew enrollment in the LEMTRADA REMS Program every 2 years from initial enrollment.
- To make available to Genzyme, documentation to verify understanding of, and adherence to, the requirements of the LEMTRADA REMS Program.

Authorized Pharmacy Representative Signature* Date*

Print Name* Title

Please fax this completed form to the LEMTRADA REMS Program at 1-855-557-2478

If you have any questions regarding the LEMTRADA REMS Program, call 1-855-676-6326

Reference ID: 3658409

genzyme A SANOFI COMPANY

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

WILLIAM H Dunn
11/14/2014